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# RECENT ADVANCES IN OBSTETRICS AND GYNÆCOLOGY

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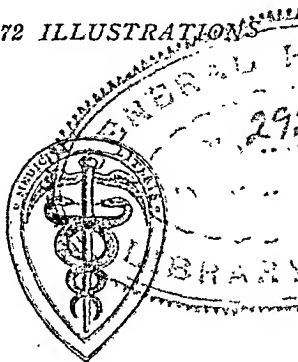
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Examiner in Midwifery and Gynaecology to the University  
of Cambridge and to the Conjoint Board.*

FIFTH EDITION

WITH 72 ILLUSTRATIONS



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## PREFACE TO THE FIFTH EDITION

DESPITE the interruption in research in obstetrics and gynæcology in almost every country in the world since the last edition of this book was published, the present edition has been brought up to date by the inclusion of one new chapter, much fresh matter in other chapters and the omission of three old chapters which could no longer be included in a book devoted to "Recent Advances." The new chapter is an attempt to describe the work of a post-natal clinic and emphasize the importance of post-natal care as a branch of preventive medicine.

In other chapters statistics and results to date have been added, and the chapter on Sex Hormones has been largely rewritten. We have been fortunate in retaining the assistance of Dr. Wilfred Shaw with his chapter on Ovarian Tumours, and of Dr. Justina Wilson with her chapter on Physiotherapy. We much regret that Dr. Courtney Gage has felt unable to continue his contributions on the use of X-rays in Obstetrics and Gynæcology. We wish to thank him cordially for all the help he has given us in past editions. Dr. Rohan Williams has joined us in the place of Dr. Gage. We are grateful to him for devoting so much time and trouble to the preparation of his chapters at a time of great pressure by other work.

A. W. B.  
L. W.

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# RECENT ADVANCES IN OBSTETRICS

## PART I. OBSTETRICS

### CHAPTER I

#### ANTE-NATAL CARE

INCLUSION of a chapter on ante-natal care in a book of this kind is desirable for several reasons. Firstly, though general, the practice of pre-natal supervision is not universal, and its more complete extension to all pregnant women is urgently necessary. Secondly, even when ante-natal care is carried out, it is often done inefficiently. Instruction on at least some of the minor points, as well as more thorough teaching of practical palpation, seem called for. Thirdly, the results of ante-natal care, which should indicate the great benefits that have been bestowed, are by no means all that is desired. Greater skill, greater knowledge and greater judgment are often required by those giving ante-natal supervision, if improved results are to be obtained. F. J. Browne (1) goes so far as to say that he believes he is "justified in saying that ante-natal care has often simply transferred mortality from one column to another. Deaths from obstructed labour are now comparatively rare, but we have replaced them to some extent by deaths from preventive operations." Any experienced obstetrician is bound to agree that there is a great deal of truth in what he says. There are, for example, numbers of Cæsarean sections, which, carrying a relatively high death rate, are yet performed, often quite unnecessarily, by relatively unskilled operators. And many other glaring examples of meddlesome midwifery, such as unnecessary induction of labour, can easily be brought to mind.

The mother is an essential social unit in our economic system, and it is the chief part of the practice of obstetrics to ensure that when a woman has a child she should emerge from the ordeal in as good a state of health as before pregnancy began, not incapacitated for her new responsibilities by an acquired physical weakness, but fit and able to carry out the vitally important duties of motherhood. A consideration of the various difficulties and

disasters of labour shows us forcibly how largely they are capable of prevention by recognition and treatment beforehand. It is this characteristic feature of obstetric emergencies which renders ante-natal supervision so promising a field of preventive medicine.

Ante-natal examination involves consideration of the following points :—

1. Previous obstetric history.
2. History of previous illnesses and general medical examination.
3. Advice on such subjects as diet, exercise, care of the teeth, regulation of the bowels, etc.
4. Measurement of the pelvis.
5. Determination of presentation and estimation of possible disproportion between the head and the pelvis.
6. Observations on the progressive increase in size of the uterus.
7. Examination of the urine and testing of blood pressure.
8. Examination for the presence of vaginal discharge or evidence of venereal disease.
9. Observation of the patient's increase in weight and of her blood picture.

The history of previous labours may be of value or entirely useless as an aid to prognosis. An account of a labour, especially a first labour, given by the patient herself is usually uninstructed and is chiefly concerned with the time it lasted, the amount of pain endured, and the length of the anæsthesia. A mere statement of the duration of labour without a knowledge of the character of the uterine contractions or "pains" tells us nothing, while the fact that "instruments" were used also does not necessarily convey any useful information. It is often impossible to analyse a history of labour, but there are certain salient facts which may be elicited from the patient or her doctor. It is well to know, for example, if the membranes ruptured early, the weight of the baby, and its condition at birth. A child weighing 6 lb., and delivered by forceps in a limp shocked condition, with considerable moulding of the head, would almost certainly point to a true contraction of the pelvis; but if a child of normal, or over weight be born in good condition, crying spontaneously at birth, and with no more than normal moulding, it is certain, however long the labour is reported to have lasted, that there can have been no disproportion between the size of the head and that of the pelvis. The commonest cause of a difficult vertex labour is the occipito-

posterior position. This point should always be remembered while listening to the story of a labour ending in severe lacerations and still-birth. Such a history does not necessarily mean that a condition was present which will give trouble in all subsequent labours. The other frequent cause of prolonged labour is that bugbear of the obstetrician, uterine inertia. This complication in a first labour will remain in the mother's memory so that she describes a prolonged and painful delivery which suggests the possibility of organic obstruction. But inertia is not likely to be repeated at her second and subsequent confinements. Such deliveries will probably be quite normal providing no other obstetric complication should arise.

One further point in the previous obstetric history about which inquiries should always be made is "Have there been any previous miscarriages or still-births?" A history of still-birth should raise the question of birth trauma, of syphilis or of renal disease; and while one miscarriage may not be of any great significance (for it is estimated that probably one pregnancy in five ends in this manner) a repetition of this would demand careful search for the cause.

If, in this search, chronic nephritis, syphilis, fibroids, badly split cervix, uterine displacement, etc., have been eliminated, and yet the woman continues to have repeated miscarriages, it is customary nowadays to regard many of these cases as due to deficiency of the corpus luteum hormone progesterone. There is evidence in support of this, for many of these cases of "habitual abortion" do show a diminished output of "pregnandiol"—the degradation product of progesterone which appears in the urine. At the same time the urine of these women also shows a diminished content of anterior-pituitary-like (A.P.L.) gonadotropic hormone and consequently a weakly positive or even negative Friedman reaction.

The acceptance of the theory that "habitual abortion" is due to progesterone deficiency has naturally been followed by the treatment—and in our view, the successful treatment—of such cases by substitution therapy. Progesterone in the dose of 5 mgm. intramuscularly may be given twice weekly. The injections should be started as early as possible in pregnancy and continued up to the twenty-sixth week. It is probably wise to stop at this time because the continuance of the injections to a later date has sometimes been thought responsible for the continuance of the pregnancy beyond the expected date of delivery.

Alternatively, the patient's own corpus luteum may be stimulated to greater activity by the administration of anterior-pituitary gonadotropic hormone. In practice one gives the "anterior-pituitary-like" hormone which is placental in origin and which can be prepared from pregnancy urine. This has the same "luteinising" gonadotropic effect as the true pituitary hormone. There are several proprietary preparations of A-P-L substance on the market. It tends to lose its activity within a short time of preparation and so it is probably desirable to use one of the varieties in which the powdered hormone is put up in one ampoule and the solvent in another. It is customary to start with injections of 30 international units twice weekly intramuscularly, increasing to 100 units (if well tolerated), the injections being again given from as early as possible in pregnancy up to the twenty-sixth week.

Another substance which is considered of value in the prevention of habitual abortion is vitamin E. This would be expected to be present in ample quantity in an ordinary mixed diet, but in cases of habitual abortion a supplementary supply in the form of a 8-minim capsule of wheat-germ oil given each day for 200 days, starting as soon as pregnancy is suspected, is considered to be beneficial. Some authors (2), however, consider that the administration should be continued until the onset of labour.

It may be mentioned here that this substance is also considered valuable in the treatment of certain cases of sterility. The dose advised is one capsule daily, continued for 200 days if pregnancy ensues.

In the history of previous illnesses, the ones about which inquiries should most carefully be made are rheumatic fever, scarlet fever, previous renal disease and the appearance of toxæmia in any previous pregnancy. This latter point is often omitted, but is most important as it is now realised that chronic hypertension frequently follows toxæmia of pregnancy which has been allowed to continue for too long a time.

The general examination of a patient is necessary for every primigravida or other patient seen for the first time. It is particularly necessary to examine the heart and lungs and to take the blood pressure. Search for septic foci is also of importance, but the only ones which might possibly play some part in the ætiology of puerperal sepsis are those in which infection by one of the pyogenic organisms, particularly streptococci, is present. The most important of these is sore throat, while others of lesser

importance would include such troubles as pyorrhœa and chronic nasal sepsis.

The question of vaginal discharge will be discussed more fully later (see p. 25), but it might be noted here that it is extremely rare for streptococci present in the vagina before labour to be in any way connected with the onset of puerperal sepsis. Such minor troubles as varicose veins may be treated even by the modern methods of injection; but if these veins first appear in the latter stages of pregnancy it is probably advisable to let treatment wait until some little while after delivery (3).

**Advice on Diet, etc.** There still lingers a popular belief that a pregnant woman should eat more than she does normally. This is quite untrue at ordinary times. But during war-time, when diets may be restricted by rationing, shortage of certain foodstuffs and perhaps poverty, there is definite truth in the statement that a pregnant woman requires more than her non-pregnant sister is normally able to obtain.

Mellanby (4) in his article on "Nutrition and Childbearing" stated that the death rate of infants in the first month of life was 33 per thousand. He gave it as his belief that this figure could be "substantially reduced by proper nutrition" for the mother, and he emphasised the greater importance of the nutritional factors in the second half of pregnancy. The League of Nations report on the "Problems of Nutrition" also stresses the importance of diet to the pregnant woman and recommends that she should be regarded as the "member of the population needing the greatest 'protection' in order to ensure adequate physical endowment for the child at birth. . . ."

The dietary requirements in pregnancy and lactation are extensively reviewed by Garry and Stiven (5) and further information can be obtained from the report of the League of Nations Technical Commission. Some of the points to which special attention needs to be paid when considering a dietary suitable for pregnancy require notice in this chapter.

(a) *Protein.* The protein requirements for a child-bearing woman are 1.5 gm. per kilo body weight according to the League of Nations Technical Commission. A lactating woman requires even more. But taking the smaller figure this means that a pregnant woman weighing 10 stones requires about  $\frac{1}{2}$  lb. of protein *daily*. In terms of lean meat, this is approximately 1 lb. The total meat obtainable in this country under war-time rationing is under 2 oz. daily! It will at once be realised that.

though many proteins of vegetable origin are not graded as "first-class," protein in one form or another is obtained from many sources other than meat, e.g., milk, fish, cheese, pulses, cereals, etc. Here is an instance of one of the many virtues of milk in the dietary to which reference will again be made, for milk protein is of the highest nutritive value and also improves the utilisation of the proteins of cereals and vegetables. Yet, despite the assistance of milk it is probable that a large number of the cases under discussion are, at the moment, receiving an insufficient amount of protein. Perhaps it will be argued that this is a good thing. But the case against excessive protein intake as the cause of eclampsia has never been clearly made out. Mellanby is not prepared to accept that idea. For if it were true, he argues that all Eskimo women, whose relative protein intake is very high, would develop this toxæmia. In any case there has never been laid against an *adequate* protein intake, the charge of being the cause of eclampsia. We must therefore conclude that there is a danger of too low protein intake at present; and that to minimise the effects of this we, as a profession, should urge that every pregnant woman should receive 2 pints of milk daily as a minimum. This is not only for its own protein, but also to assist in the utilisation of less "good" protein from vegetables, etc., as well as for other reasons, e.g., its vitamin content, as will appear later.

(b) *Calcium, Phosphorus and Vitamin D.* Mellanby says that "defective feeding of the maternal organism tends to increase the liability of the offspring after birth" to rickets. Calcium, phosphorus and vitamin D are essential to prevent skeletal decalcification and in the prevention of foetal and infantile rickets. They must therefore be supplied in adequate quantity. The average woman is balanced on an intake of 0.7 gm. Ca and 1 gm. P daily. But a pregnant woman in the last three months has, in addition to her own requirements, to supply 2 gm. Ca per week and rather less P. This supply also has to continue throughout lactation. Fresh milk contains 0.68 gm. of calcium per pint. Such a quantity of milk would suffice for the metabolism of an ordinary woman. The pregnant woman requires more and this fact constitutes another argument in support of the above statement that such a patient requires a minimum of 2 pints of milk daily. Furthermore, this would serve as a valuable source of phosphorus, vitamin D and other vitamins as well. Generally speaking, there is a world-wide tendency for the supply of vitamin D to be inadequate except in sunny seasons or in sunny climates.



It follows that it is a wise precaution in this rather sunless country for the expectant mother, even if she is getting plenty of milk, to take a small daily ration of cod-liver oil or other source of additional vitamin D. At the same time she would be receiving in the cod-liver oil, a valuable supplement of iodine and of vitamin A.

(c) *Iron*. During gestation there is a considerable drain on the maternal iron. The foetus stores it in its liver to tide it over the iron-deficient period of milk feeding. Other substances such as copper are also required for the maturation of the erythrocyte. In order to provide this iron, lean meat, egg yolk, brown bread, beans, peas, cereals and green vegetables are necessary in the diet. The addition of calves' liver once a week would supply the hæmopoietic principle and some copper. Milk, be it remembered, is deficient in iron.

(d) *Iodine*. The normal thyroid gland of an adult female contains 8 mgm. of iodine. Deficiency in this substance is not a great problem in this country but the supply of a certain amount of iodine, even here, is a necessity. This is met by eating any sea fish or by taking cod-liver oil. It should be borne in mind that apart from sea fish there is no common food which contains any appreciable amount of iodine.

(e) *Vitamins*. Vitamin A is of value as part of the defence against infection. It is of importance consequent upon the conditions imposed by the "black-out." It is present in small and variable amounts in milk; and when eggs are obtainable they also form a source of supply. But the possible deficiency would suggest again the value of a small daily dose of cod-liver, or better, halibut-liver oil, which is a rich source of this vitamin.

Vitamin B is stated to be required by a pregnant woman in considerably greater quantity than by a non-pregnant one. i.e., 5 mgm. daily instead of 1.5 mgm. This may be partly because a high carbohydrate diet increases considerably the B<sub>1</sub> requirement. Milk, eggs, pig meat, e.g., bacon, whole-wheat bread and whole grain cereals form sources of supply of this vitamin. Should there be any suspicion of deficiency some medicinal preparation containing the entire vitamin B complex, e.g., marmite or bemax, should be administered.

A severe deficiency in vitamin B is found in certain cases of hyperemesis gravidarum and therapy by massive doses of this group of vitamins is sometimes recommended. But it is probable that a shortage of this nature is a result of the vomiting and

should not be regarded as the cause. Cases of anaemia in pregnancy may also be expected to benefit by the administration of yeast. For if vitamin B<sub>12</sub> be not identical with the "extrinsic factor," the two are at least found associated, and yeast is a valuable source of these substances.

Vitamin C appears to have been endowed with less literature on the subject of its requirement by the pregnant woman than have some of the others. This is curious, as it is likely to be deficient in a war-time diet and as abortion or resorption of fetuses occurs to pregnant guinea-pigs that are kept on a vitamin C deficient diet. The increased requirement during pregnancy for Vitamin C possibly means that a gravid woman should receive up to 300 mgm. of ascorbic acid daily. One ounce of lemon juice contains some 20 mgm. of this substance. Fortunately vegetables form a more easily obtainable and more productive source of supply! But it must be remembered that the vitamin C content is impaired by long cooking, twice cooking, cooking with soda or keeping for a long time in air. Care is therefore required to see that adequate quantities of fresh and properly cooked vegetables appear in the dietary.

Vitamin D is perhaps the most important of the vitamins to a pregnant patient. It has already received adequate mention in this chapter but emphasis must again be laid on the fact that to secure a plentiful supply, a large amount of milk should be consumed daily. Failing this, vitamin D must be given as cod-liver oil, halibut-liver oil or other preparation such as "adexolin." At the same time additional calcium salts must be supplied if insufficient milk is consumed.

Vitamin E is much lauded in advertisements for its value in the treatment of habitual abortion and in fact it probably is of some value for this purpose and to increase fertility. It should be obtainable in sufficient quantity in an average intake of milk. If additional supplies are wanted the usual source is wheat-germ oil.

Vitamin K is said to be deficient in certain cases of hæmorrhagic disease of the new-born. This condition is associated with a low plasma pro-thrombin level which can be ameliorated by the pre-natal administration to the mother, for a week or two before delivery, of vitamin K or its analogues. This vitamin is also said by Macpherson *et al* (6) to be of value when administered to the child for the treatment of hæmorrhagic disease. This subject is here mentioned with the other vitamins for convenience.

To return to the question of diet. Among the substances essential to a mother and likely to be deficient in the dietary of the poorer classes even during peace time are Calcium, Phosphorus, Iodine, Iron and Vitamins A and D. It is just possible that such a deficiency may be related to the production of the toxæmias. After all, many defects in metabolism are known to be nutritional in origin. And the toxæmias are certainly manifestations of abnormal metabolism.

To eliminate these deficiencies and as a general guide, Mellanby says that the diet in pregnancy and lactation ought to include :—

2 pints of milk daily.

1 or 2 substantial servings of green vegetables *e.g.* cabbage, spinach or lettuce daily.

1 or 2 eggs or egg yolks daily.

An apple or orange or other fresh fruit daily.

Sea fish twice or oftener a week.

Calves' liver, once a week.

Cod-liver oil, 2 teaspoonsful daily if it can be taken.

The rest of the diet can be made up as the woman wishes. We need hardly add that this suggested dietary was published before the war. Nowadays, there would appear to be a further probable deficiency in the following items :—

First-class proteins: meat, cheese and egg. Vegetable proteins do not make an entirely adequate substitute.

Calcium: unless the pregnant woman can obtain and can take sufficient milk.

Iodine.

Vitamin C.

How these probable shortages can be met has already been indicated.

Water or other bland fluids should be taken freely during pregnancy, since this and the eating of vegetables, whole-wheat bread, etc., will assist in overcoming that tendency to constipation, which is so usual during this time. The question is sometimes raised as to whether alcohol is permissible. The wisest answer is that alcohol is generally inadvisable, but an occasional alcoholic drink is not likely to do any harm. In the same way, smoking in moderation cannot be regarded as definitely harmful, but it may be injudicious.

Diet may also be of importance in connection with excessive vomiting in early pregnancy. The usual advice is that something must be eaten in bed before rising, that food should be taken at frequent intervals and in small quantities, that a good deal of sugar should be included in the diet, and that fried foods should be avoided. In cases of extreme vomiting in pregnancy the value of intravenous injections of ten per cent. glucose-saline solution is becoming increasingly appreciated. Furthermore if this treatment is combined with the administration of insulin, many very severe cases are dramatically improved. Another method of treatment which is on trial is by the hormone from the suprarenal cortex. The true cortical substance is "corticoesterone" but synthetic substitutes such as desoxy-corticoesterone-acetate appear to be at least as active. A suggested dose is 10 mgm. daily. It does assist in the retention of sugar in the blood and glycogen in the liver. Such therapeutic effect as it may have is perhaps due to this. Dr. Brandstrup, of Copenhagen, reported his experience with suprarenal cortex extract at the British Congress of Obstetrics and Gynaecology in 1939 and implied that suprarenal cortex deficiency was not a primary cause of hyperemesis gravidarum but that treatment by the hormone of that gland seemed to be of value as part of the treatment of the condition. Vitamin B complex, or one or other of its components, in massive doses has also been suggested for certain extreme cases of hyperemesis gravidarum but it would appear that it is likely to be of value only in those cases of prolonged and severe vomiting which have become complicated by cerebral changes giving the clinical picture known as Korsakoff's syndrome. The pathological lesion underlying this is called Wernicke's encephalopathy. In this occur cranial nerve palsies, mental changes and retentus. In such cases vitamin B<sub>1</sub> (Riboflavin) in large intravenous doses may be of value. Others think that huge doses, e.g., 50 mgm. of Vitamin B<sub>1</sub> (Aneurin) are preferable. Such extreme cases of vomiting are, however, very much the exception, and in the more usual case treatment by suggestion, isolation from sympathising relatives, gradually increasing diet, etc., perhaps reinforced by intravenous glucose and insulin nearly always produces a cure, particularly if it can be impressed on the patient that the induction of abortion, which is often her object, is not going to be performed. Despite such assurance to the patient, the doctor may be forced in certain extreme cases to give consideration to the question of terminating pregnancy. But we

feel that far more pregnancies are terminated from pressure by the relatives and from sympathy than are ever really indicated on strictly medical grounds.

**Exercise.** One cannot enter into a detailed discussion on this matter. It is sufficient to say that walking is the only exercise without any undue risk of miscarriage; and that, particularly in patients who have had previous miscarriages, long distance or fast motoring should be avoided, and coitus abstained from at about the times when the monthly periods would normally have been due. The subject of overseas travel may conveniently be considered at this point, since it is a question that is frequently asked of the doctor. The actual crossing from England can hardly be forbidden as being definitely likely to cause a miscarriage, but if patients undertake such a journey they must realise that crossing by boat is risky, particularly if the weather is rough; approximately the same risks are attached to flying.

**The Teeth.** It is popular knowledge that the teeth decay very rapidly during pregnancy, and therefore gravid women must be advised to see the dentist at least three times during the period of gestation. Furthermore, inquiries should be made as to the adequate supply of calcium in the diet, and it is probably a sensible precaution against dental caries for every such patient, however adequate the diet, to take each day some proprietary preparation containing calcium and vitamin D.

**Measurement of the Pelvis.** Pelvimetry is one of the subjects in which recent advances have been made in our knowledge, even since the last edition of this book, and they still continue to be made. Pelvimetry by the X-ray has been brought to a fairly exact science, and in the hands of the expert an accurate measurement of the brim and of the outlet can be obtained. Chassar Moir (7) has recently published an interesting survey of the present position and has indicated how a well-equipped hospital can avail itself of the information which can be obtained by modern methods. But even under these ideal conditions, cephalometry is very far from being accurate. Therefore the exact determination of any possible disproportion by radiological methods is not feasible and investigation of ante-natal cases by this means will not entirely solve the difficulty of estimating overlap. Moreover, in the vast majority of cases radiological investigation is not necessary, particularly as it involves special apparatus, the services of a very expert radiologist, and considerable expense. It should be a fairly simple matter by clinical

methods to divide obstetric cases into those in which the pelvis is of good size and clearly offers no difficulty to the passage of the child; and those in which such an easy labour can hardly be expected. It may be thought that the pelvis is small or the child is big. In either event, this is the case that should be referred to the expert obstetrician for his opinion and he, more and more, will be glad to receive assistance from the expert radiologist.

In the routine management of a case therefore one usually is content with the old clinical methods, but we believe that the external measurements should really be regarded as valueless. Admittedly the use of calipers has to be taught to students because they are still asked about them in their final examinations, and because the woman who is going to have a baby rather expects to have some measurements taken with this instrument. We would suggest, however, that, even if these measurements are taken with all due ceremony, no deductions should be drawn from them. We think that the possibilities of error, both in measurement and in deduction, are so great that no value can be attached to external pelvimetry.

*The Internal Examination of the Pelvis.* It would appear that external pelvimetry was devised in order to obtain some information, however inaccurate, as to the size of a pelvis through which a baby had to pass. At the time of their invention the more accurate investigation by internal methods was often resented in those earlier days of ante-natal care, and the external methods have been preserved. Nowadays, however, all gravid women of at any rate the better educated classes expect a vaginal examination to be made during pregnancy, and at this examination the internal pelvic measurements should be taken. In time this may come to be replaced by routine X-ray pelvimetry and cephalometry. But that time is not yet. And it must be remembered that it requires expert knowledge and technique to do exact X-ray pelvic mensuration. So clinical methods still survive and with practice the trained examiner can form a very accurate estimate of the size of the bony birth canal, brim, cavity and outlet. But the examination should not be made too early. If it is postponed until the twenty-eighth week, or even a little later, the softening of the vagina, etc., has become so well established that the internal measurements can be ascertained with the minimum of discomfort to the patient. Many obstetricians leave this internal examination until, say, the thirty-sixth week. This may perhaps be rather too late, for if some abnormality be dis-

covered. the short notice of the enforced alteration in the patient's arrangements may be resented. The student is taught to measure the diagonal conjugate with two fingers in the vagina, but one more experienced can usually learn all that is required with considerably less inconvenience to his patient if only one finger is used. It must be emphasised that it takes months or years of practice before anyone can claim really to have learned something of the size and shape of a given pelvis from an internal examination. With further experience the one-finger method will be found to yield the fortunate possessor of fairly long fingers equally accurate information. Whether one finger or two be used the pelvis should be explored in all directions for a distance of  $4\frac{1}{2}$  in. from the lower margin of the symphysis pubis. It is only the expert, however, who can approach the internal pelvic measurement by this method of systematic regional exploration. and the more usual practice is to place the tip of the examining finger or fingers against the lower part of the sacrum and to follow this up as far as possible. The sacrum should be lost above its middle piece and in the normal pelvis the promontory should be out of reach. If, however, the pelvis is of the generally contracted type, the whole of its anterior surface may be palpable at this examination. In the case of a flat pelvis, although part of the anterior surface of the sacrum may be bowed backwards out of reach of the finger, above this bony concavity, the overhanging promontory can be felt projecting into the brim. If a finger is next placed on the back of the symphysis, the brim can be traced from before backwards: but here again the normal brim should recede beyond reach of the finger at about the coronal plane. The cavity of the pelvis should now be explored, but very considerable experience is required before any estimate of the actual measurements can be taken as even approximately correct. However, gross variations from the normal, the presence of any abnormal mass such as a tumour likely to obstruct labour, or an undue mesial projection of the ischial spines, would easily be recognised. The outlet is a more simple matter. An approximate idea of the width of the sub-pubic arch can be obtained by pressing the index finger upwards into this arch on either side of the urethra. In the normal woman there will be found ample room for this manœuvre, but in cases of narrow arch a feeling of restriction will be experienced. Measurement of the inter-ischial diameter can be made with calipers, but a measurement accurate enough for all practical purposes can easily be

obtained by pressing the flexed knuckles of the first inter-phalangeal joints into the space between the ischial tuberosities. It should be noted here that when this measurement is first made the examiner tends to put his knuckles too far forwards. With greater experience he will find that his knuckles need to be at, or even behind, the anus if the full width of the inter-ischial diameter is to be appreciated. In the normal pelvis four knuckles of even a moderately large hand should easily fit in. But it is not uncommon to find a slight contraction in this diameter, which may then accommodate only with difficulty the four knuckles above referred to. Such cases of minor contraction of the outlet may lead to some difficulty at this level, but care must be taken not to over-estimate the amount of difficulty likely to be met. The difficulty is due not only to the hindrance to the advancing head offered by the narrowed transverse diameter but also to the fact that the narrowed pubic angle which is inevitable in this deformity, prevents the broad occipital end of the foetal head from sitting well up into its arch. Instead, it pushes the head caudally and so causes undue perineal stretching, consequent delay and the risk of severe laceration. We must admit that on very rare occasions examples of extreme contraction of the outlet are encountered, as for example in cases due to the pelvic deformity resulting from tubercular caries of the lower dorsal or lumbar spine during infancy. But, let it be repeated, such cases are very rare. It can be taken as a rule that in the relatively common pelvis which shows some mild contraction of the outlet, whether it be a generally contracted pelvis or one slightly funnel shaped, if the head of a foetus will demonstrably enter the brim it is capable of being delivered through the outlet of that same pelvis, though perhaps with some difficulty. This is a clinical fact which remains true even if it is confirmed that, as maintained by Chassar Moir (7), the antero-posterior is the contracted diameter in those cases in which the pelvis becomes smaller towards the outlet. And though cases of antero-posterior contraction at the lower pelvic strait do undoubtedly occur most obstetricians appear to follow Whitridge Williams in considering that the common deformity in this position is a transverse contraction.

In the above description it will be noticed that the old-fashioned classification of contracted pelvis has been adhered to. Of recent years, however, radiological study of the bony pelvis has shown us that the older classification is not in every way satisfactory and a new classification has been suggested. This new one is not yet



universally accepted and indeed, considerable criticism can be levelled at it. But it does introduce a new line of thought and may modify our conception of the mechanism of delivery in certain obstetric cases. We owe this new concept of the female pelvis to Caldwell and Moloy (8) who described four parent types of pelvic shape and whose work will receive further and fuller discussion from

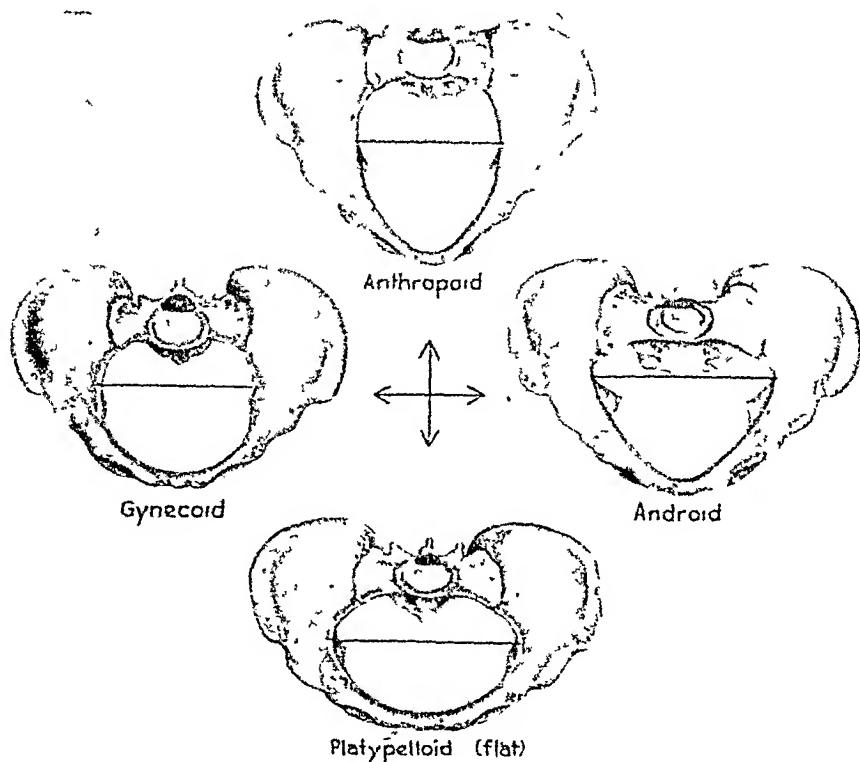


FIG 1. Characteristic inlet of the four parent types of pelvis.  
(Caldwell and Moloy).

the radiologist's point of view in the chapter devoted to X-rays in Obstetrics. A slightly modified classification was presented by Thoms (9), but the former classification is the more usually accepted and is briefly as follows: the four basic types are (1) the anthropoid, with a long oval shape, the long diameter being antero-posterior: (2) the gynæcoid type, which is the normal round female pelvis; (3) the android type, which is male in its characteristics and shows a flat posterior segment from side to

side and a curving or pointed anterior segment ; in fact this type of pelvis may be said to approximate to a triangle, the base being posterior ; (4) the platypelloid pelvis which is "flat," i.e., the transverse diameter exceeds the antero-posterior.

In between these four parent types they describe also four or eight intermediate stages such as "gynæcoid type with anthropoid tendency," "gynæcoid type with platypelloid tendency," etc.

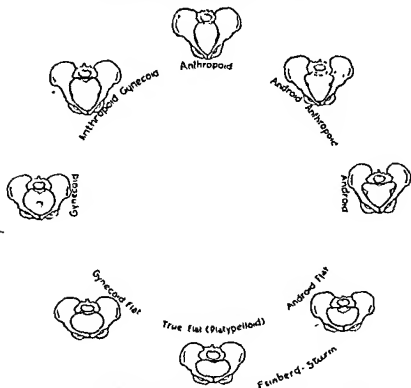


FIG 2 Diagram showing shapes of pelvic brim intermediate to parent types

One of the possible practical results of this knowledge about the variations in the pelvic shape is that one may find a pelvis which would allow easier delivery to certain cases in some manner different from the standard obstetric mechanism. Thus one can imagine an "android pelvis with anthropoid tendency" in which the narrow anterior segment, the long antero-posterior diameter at the brim, and the relatively broad posterior segment would

allow easier passage to a head in the occipito-posterior position than it would to one in which the occiput was forward or in the obliquely anterior direction.

Caldwell and Moloy have performed this service to obstetrics—they have indicated that the shape of the pelvis is a morphological characteristic rather than an acquired phenomenon. Consequently a variation from the normal gynæcoid pelvis indicates an inherited tendency and not, usually, a deformity resulting from disease. They have shown that except in real rickety cases, the flat pelvis is not so common as used to be thought and that the mild funnel pelvis, which is now described as android, is of relatively frequent occurrence.

But the identification of these pelvic shapes requires X-ray examination, preferably by some specially adapted apparatus. Caldwell and Moloy employ a specially designed technique which enables them to examine stereo-roentgenograms in their "Precision stereoscope." As an instance of the elaborate routine investigation it may be mentioned that among the criteria required for the diagnosis of an android pelvis is narrowing of the sacro-sciatic notch as demonstrated in a lateral roentgenogram.

Let us agree that all this is an advance in our knowledge and that the antero-posterior shortening of the posterior half of the pelvis which is indicated by narrowing of the sacro-sciatic notch is perhaps as important as any. But we are a long distance from having the necessary facilities for the routine X-ray examination of all antenatal patients. Even if we did have such facilities, Ince and Young (10) suggest that "the attempt to classify the shape of the pelvic brim merely by subjective impressions into ten or twelve classes as suggested by Caldwell and Moloy is not only unscientific but results in a classification which is cumbersome and of no practical value." They go on to say that there seems "to be valid reasons for preserving the accepted classification into flat and generally contracted pelvises rather than for adopting the suggested types of Caldwell and Moloy, which rely too much on impressions of the shape of the pelvic inlet." But they do stress the importance of diminution in the size of the outlet and diminution in the size of the sub-pubic angle as indicating that forceps delivery will probably be called for; and accurate knowledge concerning these points is best obtained by an expert radiologist, though the clinician should not be far behind.

We may sum up thus: in ordinary obstetrics and for teaching students the old conception of difficulty in the antero-posterior

diameter of the brim in a flat pelvis; difficulty all the way down in a generally contracted pelvis; and difficulty in the transverse diameter of the outlet in cases of funnel pelvis will prove the most easily understandable conception of the position. But for the fortunate people who work in hospitals with elaborate modern apparatus and who have the benefit of working with radiological experts, the morphological classification is probably a step forward. These favoured ones can also obtain highly accurate pelvic measurements—much more accurate than the ones ordinary clinicians have to be satisfied with. But ordinary clinicians when they have gained experience can usually foretell with surprising accuracy what will be the clinical ending to any given obstetric problem. The most highly equipped obstetric department still fails to get accurate measurements of the foetal head; and nobody can prophesy how the uterus will act and how it will be able to mould the foetal head so as to overcome mechanical difficulty. So we shall continue to have obstetric problems. But—a strong point in favour of an adequate X-ray department in every obstetric hospital—the radiological study of such problems during labour will often yield information which will help in finding the solution.

Determination of the presentation is not really necessary until about the thirty-second week of pregnancy, for prior to this time changes from day to day are by no means uncommon. As will be referred to at greater length in the Chapter on "Breech Delivery," it is necessary to know how the child presents at the thirty-second week, for if a malpresentation should be present, the optimum time for the performance of version can then be selected. Should great variability of presentation be noticed at the thirty-second week and at the subsequent antenatal inspections, it is prudent to suspect the existence of an abnormality which prevents the head engaging in the brim, such as a contracted pelvis (even if this has not been previously discovered by mensuration), placenta prævia, or twins. If, on the other hand, the first vertex position is found consistently present with the head engaged in the brim and well flexed, spontaneous alteration from the normal is not likely to occur. Although British text-books only describe four positions of the vertex it is frequently found that the child lies with the back to the mother's side, *i.e.*, midway between the anterior and posterior positions, especially about the thirty-sixth week. This, the left or right occipito-lateral position, persists if there is any

shortening of the antero-posterior diameter of the pelvic brim, up to and during the first stage of labour.

An attempt should always be made to estimate the degree of flexion of the presenting vertex, and little experience is needed to appreciate that when the head is well flexed the sincipital end of the foetal head is felt at a higher level in the mother's abdomen than is the occipital end. In other words, that portion of the foetal head which is felt higher up should be on the side of the mother's abdomen which is opposite to that on which the foetal back is found. If good flexion of the vertex exists then there is little hesitation during the labour in forward rotation of the occiput; even in occipito-posterior cases a well-flexed vertex can be expected to show a long forward rotation of the occiput and to terminate in easy delivery. Further, even if a slight degree of pelvic contraction be present, providing good flexion exists, the head is in the most favourable attitude to overcome any difficulty that may be experienced.

The question may be asked, "Can anything be done antenatally to prevent the occurrence of the occipito-posterior position during labour?" It must be agreed that the routine application of Buist's pads does succeed in converting more cases of occipito-posterior presentation to that of occipito-anterior than would occur spontaneously without their use. But the number so benefited is relatively small, and most obstetricians seem to be of the opinion that the application of pads as a routine is inadvisable. The good that they do is probably more than counterbalanced by the harm caused in the form of physical discomfort and mental anxiety.

*The estimation of possible disproportion* between the head and the pelvis is one of the most difficult things in obstetrics. In the vast majority of cases the head will be found to engage spontaneously in the pelvic brim, or to be capable of being pushed down so that the absence of disproportion is conclusively demonstrated. But in others the high position of the head and the fact that by simple pressure it cannot be made to fix in the brim suggests the possibility of disproportion. The more experienced the obstetrician the less mistakes he will make in estimating the degree of difficulty to be anticipated. But even the most skilled observer is capable of being deceived. Every doctor with much midwifery practice must be able to remember cases in which a small pelvis and a seemingly big head appeared to promise grave difficulty, and yet, when labour came on, the

uterus, acting perhaps in a specially efficient manner, was able to bring about delivery of the head with apparent ease. It is because this sort of thing has happened so often that obstetricians have come to realise that there were cases in which even the most experienced could be mistaken in the matter of prognosis—that examples appeared from time to time when expected difficulty did not materialise. It follows in such cases, that if induction of premature labour had been performed with the idea of preventing this difficulty, the induction must have been unnecessary. There then arose a tendency to think that the induction of premature labour in primigravida for supposed disproportion was a practice no longer to be permitted. Instead, it was argued, the woman should be allowed to go into spontaneous labour at term, to undergo what is called a “trial of labour.” Such a tendency was, in fact, the natural reaction against the excessive number of inductions of premature labour, and worse, Cæsarean sections, which were performed often on far too flimsy evidence of pelvic contraction or of disproportion. The official obstetric attitude towards a case of disproportion in a primigravida thus developed into this: that all such cases should be treated as trials of labour except when the pelvic contraction was manifestly of such an extreme degree as to be patently insuperable; and that on the results of the trial, the judgment of the correct conduct of any subsequent pregnancies and labours should be based. If, as usually proved to be the case, the head went through easily, then spontaneous labour at term could be anticipated in the future; if there was difficulty, perhaps successfully overcome after a struggle, then induction of premature labour for subsequent pregnancies would be advisable; if there was great difficulty, severe maternal or foetal damage, or if the trial had to be given up as a failure and delivery secured by Cæsarean section, then this operation would again be required in the future.

The main points to be remembered in regard to trial labour are as follows. No vaginal examinations may be made. The patient must be kept in a condition as aseptic and as safe for Cæsarean section at the end of, say, twenty hours of labour as she was at the beginning. This would necessitate that the progress of labour should be watched by abdominal examinations only, and that to prevent the possibility of droplet infection anybody going near the patient must wear an efficient mask. Furthermore, the progress of labour must be judged before the patient has been allowed to continue for too long and so become exhausted. The

decision whether to allow the labour to progress or whether to do a Cæsarean section must be reached before the patient has become dangerously tired. But a trial of labour must not be deemed a failure until after the membranes have been ruptured for at least two hours, during which time the patient has been having good pains seemingly of the second stage type.

Thus it will be seen that trial labour demands that the place in which it is conducted shall be worthy of the trust that the preservation of complete asepsis can be maintained; that the obstetrician in charge must be a man of skill and experience; and that it must be possible to do Cæsarean section under reasonable conditions if required. Many obstetricians therefore think that "trial labour" is probably excellent in institutional treatment and in really first-class nursing homes. But in domiciliary midwifery and in nursing homes not quite up to the above standard, the risks of introducing minor sepsis by the induction of premature labour may be less to be feared than are those attached to a difficult trial labour under conditions that are not quite perfect.

Therefore we can return to the question of estimation of disproportion. In cases without disproportion the fact that the head can be forced into the pelvic brim can easily be demonstrated by fundal pressure or by making the patient sit up. In cases of greater difficulty however, direct pressure applied to the head has to be employed, and each obstetrician must work out his own technique for this. He will also perhaps find that the bi-manual method as suggested by Munro-Kerr may help him, though others have given up this manœuvre. Whatever method he may employ he will find that the absence of disproportion is usually demonstrated by the fact that, by whichever technique has been employed, the head has been forced to engage in the brim. In other cases he will think, possibly wrongly, that disproportion is present. If really definite and undoubted disproportion is demonstrable before the thirty-sixth week, then, if the trial of labour doctrine is not being strictly adhered to, most people would agree to let the case go to within a few days of the expected date of labour and then to do Cæsarean section. If at the thirty-sixth week no disproportion is demonstrable, the patient should be examined at weekly intervals to ensure that this satisfactory state of affairs still exists. If at one of these examinations the obstetrician thinks that disproportion has become evident, he will, if he conforms to modern standards, assign the case to the group to be treated by a trial of labour. Alternatively he may be content to let

the pregnancy continue for, say, another week and then to examine again under anæsthesia. If at this examination he still finds that there is some, though a minor, degree of disproportion, and if he is one of those that still prefers to induce premature labour in these cases, this operation will be carried out under the same anæsthetic.

It may be repeated that the moderns do not agree with this line of treatment and will wait until the patient comes into labour and then observe the case at a "test" in the manner described above. And it must be admitted that experience teaches that trial labour so generally results in spontaneous delivery when difficulty had been expected, that induction of premature labour in a primigravida on the grounds of disproportion is to be deprecated unless the patient's environment precludes the adoption of the more modern practice.

**Observation of the Progressive Increase in Size of the Uterus.** It is useful during pregnancy to keep a watch on the size of the uterus and to observe that it agrees with the size it should be at the particular date during pregnancy at which the examination is made. For if the uterus is found to be bigger than would be expected for the duration of pregnancy, then an investigation into the diagnosis between error in dates, hydramnios or multiple pregnancy, must be made. If, on the other hand, the uterus is found to be smaller than would be expected, the suspicion of possible dead pregnancy may be aroused, or again the patient may be wrong in her dates.

Admittedly there are possibilities of very considerable error in any estimation of the duration of the pregnancy by the height of the fundus. This height is dependent, not only on the duration of the pregnancy, but also on the presentation, the amount of liquor amnii, the attitude and size of the child, etc. Furthermore, an attempt to date the pregnancy by seeing how the height of the fundus corresponds with the position of the umbilicus is introducing an unnecessary source of error since this structure is subject to such variations in position. It seems to us better to take the tip of the ensiform cartilage as one landmark and the top of the symphysis as the second. Next, a small circle is drawn on the woman's abdomen marking where the umbilicus *should* be, *i.e.*, with its upper margin immediately beneath the half-way mark between the symphysis and the ensiform.

The fundus at the thirty-sixth week should be at the tip of the ensiform cartilage, and at the twentieth week of pregnancy the



fundus should reach the lower margin of where the umbilicus ought to be. The progress in the intervening sixteen weeks is regular, and therefore by dividing the distance between these marks into halves, quarters, etc., the position at which the fundus of the uterus should reach at any given date from the twentieth to the thirty-sixth week can easily be indicated (see Fig. 3).

Similarly below the umbilicus : the fundus by about the twelfth week should be palpable about three fingers above the symphysis. From this twelfth week mark to the twentieth week is a period of eight weeks which again is easily divisible into two, thus indicating the height to which the fundus should reach at the sixteenth week.

In addition to the points in connection with which a knowledge of the height that the uterine fundus has reached at the various weeks in pregnancy is useful, can be included the subject of post-maturity. If this diagnosis is ever clearly established it is the duty of the obstetrician to induce labour, because senile changes in the placenta may result in foetal death during, or even before, labour.

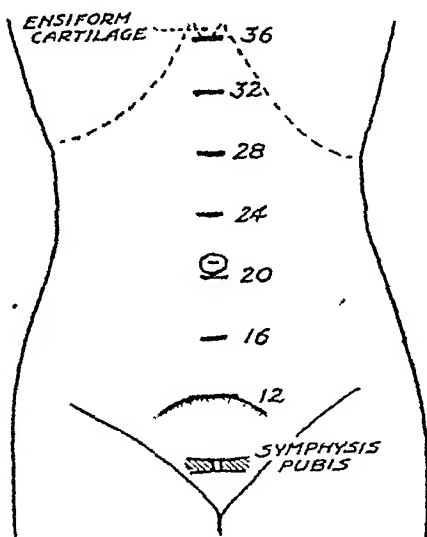


FIG. 3.

But before such interference would be advisable the two following criteria of post-maturity should be demonstrable :—

- (a) The patient should be clear about her dates, and from these dates the expected date of confinement is fixed.
- (b) This expected date of confinement has been confirmed by the uterus having conformed to the size it should have been at the various weeks of pregnancy when examinations were made.

Even so one does not make the definite diagnosis of post-maturity with its consequent induction of labour, until three weeks beyond the date thus fixed has passed. But induction may have been decided on during this three weeks if, in addition to suspect post-maturity, disproportion may also have been suspected.

**Examination of the Urine and Testing of the Blood Pressure.** This can be put very shortly. The urine and blood pressure should be tested when the patient is first seen, and thereafter it is advisable to test the urine every fortnight from the twentieth to the thirty-second week, and thenceforward, weekly. Every time the urine is tested the blood pressure also should be recorded. It is probable that many of us will resent this additional work. But frequent readings of the blood pressure are important in all cases, and essential if there be any suspicion of toxæmia. Readings from 125 to 135 are usual, though in debilitated women a low pressure, sometimes below 100 mm., is found. A rise in the diastolic blood pressure usually precedes a systolic rise and is one of the earliest signs of developing toxæmia. The systolic rise shortly follows and a case exhibiting a systolic pressure of 140 mm. or over and a diastolic that has previously risen to 90 mm. or more should be regarded as suspicious. In fact, with the exception of too great increase in weight (*vide infra*) this steadily climbing blood pressure is the earliest sign of toxæmia of pregnancy.

The urine testing, etc., should greatly have diminished the incidence of eclampsia, but unfortunately this decrease has not been as striking as one would have hoped. For it is possible for eclampsia to supervene on a very short stage of albuminuria. It is probable, however, that even if the results in regard to the prevention of eclampsia have not been all that could be desired, the discovery of albumen in the urine of a pregnant woman and the institution of suitable treatment for her case may be expected to carry an alternative benefit, namely, a diminution in the number of women who might otherwise have sustained damage to the cardio-vascular-renal system due to prolonged albuminuria of pregnancy.

With regard to the method of taking a specimen, the patient should be instructed to sponge the vulva before micturition and to pass water in two portions, rejecting the first portion. If albumen is found, a catheter specimen should be examined, and if albumen be present in this, further examination by the microscope for pus is necessary in order to eliminate the possibility of pyelitis or cystitis.

Glycosuria is not uncommon during pregnancy, and sugar should therefore be tested for as a part of each urine examination. If sugar be found it should be investigated by a fermentation test or by the ozazone test, to see whether it is glucose or lactose.

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If the latter, its presence can be ignored; but if the former a blood-sugar curve should be done to see whether the glycosuria is, or is not, of clinical importance.

**Examination for the Presence of Vaginal Discharge or Evidence of Venereal Disease.** Gonorrhœa and syphilis, either separately or together, may co-exist with a pregnancy. The presence of a purulent discharge should always excite a suspicion of gonorrhœa, particularly if vulvitis is present or if there is pus in the urethra.

But it must be emphasised that the diagnosis of gonorrhœa cannot be made by a mere clinical examination. It is necessary that smears and cultures should be taken and sent for examination by a competent and careful bacteriologist, and that a complement fixation test should be carried out.

In taking the smears the urethral orifice should be exposed and carefully cleaned. The urethra is then "milked" by squeezing it from above downwards by a finger in the vagina. The bead of pus that appears at the orifice is picked up on a coated probe, or, far better, a platinum wire loop, and then made into as thin and as flat a smear as possible on a clean microscope slide. It is desirable at the same time to inoculate the appropriate media with some more of the urethral discharge in the hope of obtaining further information from cultures.

In the same way a smear from the cervix is made only after exposing and cleaning the outer surface of the cervix with the utmost care. If a tubular speculum is being used, the cervix can now be squeezed between the end of this and the sacrum, and a bead of secretion will be pressed down the cervical canal to appear at the external os, whence it is picked up and spread to form a smear as before. Again, culture media should be inoculated with a further specimen of the discharge, this time from the cervix.

It is important to realise that carelessly taken specimens and badly made smears are quite useless. Also that in long-standing cases it often requires several smears before the gonococcus can satisfactorily be demonstrated. *Never take a single negative bacteriological report as excluding gonorrhœa.*

During pregnancy the clinical signs of the disease frequently become accentuated, while if contracted during pregnancy the infection is liable to be very severe. In any case all pregnant women infected with gonorrhœa, and indeed all cases of purulent discharge during pregnancy, must be treated. Otherwise there is danger of infection of the child's eyes.

In this treatment we have now the valuable assistance of the sulphanilamide group of drugs. Perhaps the most useful for these cases is May and Baker's "693," which can be used in the treatment of pregnant as well as non-pregnant women. It of course entails the same risks in both cases. Whenever large dosage or prolonged therapy is required there is the risk of causing agranulocytosis. Minor toxic symptoms are of less importance and if "693" causes excessive vomiting it may be found that sulphanilamide is better tolerated. But if there is the slightest indication of a commencing leucopænia all drugs of this type must instantly be stopped.

In addition to chemo-therapy local treatment is also of value and in order to minimise the danger of abortion, applications to the cervix and urethra are preferable to vaginal douches. For example, on alternate days the urethra should be cleaned as described above, and then a probe or "wooden applicator" with the end coated with cotton wool and dipped into 10% protargol, or 5% argyrol, is introduced and allowed to remain for a few seconds. Then the cervix is cleaned, not only outside but also in the cervical canal, and a similarly prepared probe dipped in 2% acriflavine in glycerine is passed into the cervical canal and kept there for a short time. It is also of benefit occasionally to follow this up by introducing into the canal, and retaining it there by means of a vaginal plug of iodoform gauze, a medicated bougie such as one sold under the name of "Spuman."

In resistant cases, vaccine treatment can be used without undue fear of abortion. Small doses should be given at first, *e.g.*, 0.2 c.c. of the St. Mary's Hospital mixed gonorrhœa vaccine, increasing by 0.1 c.c. at weekly intervals.

Other causes of discharge during pregnancy are thrush (monilia) and trichomonas vaginalis. The latter can often be diagnosed by the profuse, slightly greenish discharge containing bubbles. But its real recognition depends upon finding the flagellate protozoon in hanging-drop preparations of the diluted discharge. It is treated by lactic acid douching and by the insertion of "stovarsol" tablets in the usual way. Thrush often exhibits a characteristic picture. There is an extremely profuse, thick paste-like or curdy discharge. Many have seen a vagina containing great quantities of such a discharge and not realised that thrush was the underlying cause. The other type of monilial infection, in which white patches are found on the vaginal walls and in the vaginal vault, are, in our experience, more common in

young girls who are not pregnant. In either type, the bacteriological investigation requires care and experience. The vaginal wash method described by Liston and Cruickshank (11) may be found useful. The sediment from the washings, on being mixed with a drop of watery solution of methylene blue and examined under the microscope reveals long strands or hyphæ of the mycelium of *oidium albicans*. These do not stain but are refractile. Other highly refractile, almost pear-shaped bodies are the blastospores of the fungus. Once the condition is diagnosed it can be cured with almost dramatic suddenness by cleaning away the discharge and thoroughly swabbing the vagina on one or two occasions with a 2% aqueous solution of gentian violet.

*Syphilis* may be suspected from a history of premature stillbirths or of the birth of a macerated foetus; or it may be discovered by finding a positive Wassermann reaction in a woman who is attending an ante-natal clinic where this test is done as a part of the routine. It is remarkable that in clinics where this does occur a figure usually between 2 and 5% of positive reactions in previously unsuspected cases is found. And though doubt has been thrown on the validity of these results, since it is contended that the accuracy of the test is vitiated by the presence of a pregnancy, it must yet be accepted that many cases of unsuspected syphilis do exist. In a recent publication (12), however, the percentage of positive reactions found was only 0.47% of 1,496 primigravidæ, and 1.31% of 1908 multiparæ.

If syphilis be suspected from the history or from any other details revealed by the patient or her husband, a Wassermann test of both husband and wife should be done at once.

When a pregnant woman is found to have syphilis she must receive anti-syphilitic treatment; and it can be said that it is never too late to institute this treatment which is strikingly successful for the foetus *in utero*.

But if one is to be really sure that the baby is uninfected there must be thorough anti-syphilitic treatment for the mother throughout the period of gestation, particularly in the second and third trimesters.

In fact, if a woman has ever had syphilis, however well she was treated, however soon her Wassermann reaction became negative, and despite the persistence of that negative reaction, that woman requires full anti-syphilitic treatment throughout every successive pregnancy if an uninfected baby is really to be made as certain as is humanly possible.

**Weight during Pregnancy.** The average increase in weight during pregnancy is 16 to 18 lb. (13). The monthly gain during the second and third trimesters is normally between 2 and 4 lb. An increase of 5 lb. or more per month is indicative of water retention and is suggestive of an impending toxæmia. Furthermore, the likelihood of development of toxæmia seems to be especially indicated in the event of a sudden increase in weight. It therefore would seem advisable that every patient should weigh regularly throughout pregnancy and should be instructed to report at once to her doctor if the monthly increase is 5 lb. or more.

**The Blood Picture in Pregnancy.** It has long been known that blood dilution occurs normally in pregnancy, and it would appear from many articles (14, 15, 16) that in women of the poorer classes an iron deficiency is often manifest. This appears to be due partly to a diet poor in iron, and partly to the loss of iron during reproductive life. Theoretically, therefore, it would seem advisable to have a blood count, or at least a hæmoglobin estimation, done on every pregnant woman, but it will probably be considered adequate by most to have this test made only if any suspicion of anæmia is aroused. It is fortunate that in this country only the milder forms of microcytic anæmia are likely to be encountered, though in tropical countries anæmias of the pernicious type are relatively common. Whether a war-time diet with its possible shortage, among other things, of B<sub>12</sub> vitamin (which implies a shortage of the identical, or at least associated, "extrinsic factor") will result in an increase in the anæmia of pregnancy in this country yet remains to be seen.

Should a hæmoglobin deficiency be discovered it will probably respond rapidly to the administration of large doses of iron. In the occasional resistant case an associated deficiency in the gastric hydrochloric acid may be discovered and may call for treatment. It is possible that some especially severe cases will benefit from a blood transfusion and in the rare cases of macrocytic anæmia liver extract will of course be administered.

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## CHAPTER II

### POST-NATAL CARE

IN addition to all that we understand by "Public Health," obstetrics has been more activated by the principles of prevention of disease than any other branch of medicine. It showed the way in the early part of the century by the development of ante-natal care. If it has been disappointing in effecting the great improvements which were originally expected with so much confidence, yet it has done a great deal, and its mistakes have been those of detail and method rather than those of principle.

Ante-natal care and treatment is concerned directly with prevention of ill health in pregnancy and abnormality of labour, and only indirectly with the maintenance of the woman's health after the puerperium. This can be largely ensured by post-natal attention and treatment where necessary.

New, but quite obvious ideas seem to dawn slowly on the human mind. With so much attention, in a thousand clinics and laboratories, devoted to the pathology and treatment of obstetrical conditions, it is curious that recognition of the value of post-natal attention has taken so long to be appreciated. Even yet it is patchy in its organisation and imperfect in its execution.

The tardy development of post-natal medicine is not due to any lack of its value for the health of women, but to our failure to realise the overwhelming importance of prophylactic medicine in general. Working on the statistics of London hospital out-patients in the gynaecological departments, and the figure of 30% of attendances being directly due to the morbid results of childbearing, the writer has calculated that one woman in every nine who have had children has some form of disability directly resulting from childbirth which makes her seek hospital advice. This calculation leaves out of account all those women who suffer from some non-gynaecological condition, such as abdominal proptosis, sacro-iliac strain, and anaemia who attend medical or surgical out-patient departments.

So long, therefore, as pregnancy and labour are the cause in one way or another, of so much ill-health, there is a very wide field for the post-natal examination and correction of these conditions which can spoil the vigour of a woman's life for many years. It is curious that, in the face of so much evidence of the



established and neglected results of childbearing which is daily before us, that post-natal work has aroused comparatively little interest. The fact is recognised in official quarters. The Chief Medical Officer to the Ministry of Health wrote in his Report for 1938 :—

“ It is being more widely recognised that much ill health and disability follow neglect of conditions resulting from childbirth which are capable of cure or amelioration, and need not be accepted and patiently endured. Post-natal work is still, however, a relatively neglected field of preventive medicine.”

The chief criticisms which can be made at present are : (1) the relatively small number of organised post-natal clinics and small amount of real post-natal work in private practice ; (2) the crumby and uninstructed nature of the work already carried on in both clinics and private practice ; (3) the failure of the mothers to present themselves for examination, and treatment if necessary ; (4) the lack of facilities for treatment on an adequate scale.

As we have suggested, not only are the clinics too few in number, but the work suffers in quality. There is still too much emphasis on purely pelvic conditions, some of them comparatively trivial, and not enough attention is devoted to the orthopædic and medical aspects of the patient's condition. A large number of women certainly suffer from leucorrhœa, cervical lacerations and retroversions, but there is also a great deal of pain and vague but serious disability due to joint strain, muscular relaxation of the abdominal wall, and anæmia. So long as the vaginal speculum remains the typical instrument of the post-natal clinic, there will be relatively little attention given to the woman's general condition. Again, sub-involution of the uterus is remembered by all in charge of these clinics, but it is forgotten that the patient may be suffering from sub-involution of other parts of her body such as the perinæum, muscular system, joints, veins and even thyroid. Pregnancy is a time of “ evolution ” of nearly all the systems of the body under the intense stimulus of an increase in endocrine activity. During the puerperium a corresponding involution of all these activities should normally take place. Any of them may fail to regain the status quo ante, which prevailed before pregnancy began, with the inevitable result that the woman's health will be impaired, perhaps for years after her confinement. It is the work of post-natal care to discover and correct these sub-involutions. A further difficulty which interferes with the

maximum benefit which could be obtained from post-natal work is the reluctance of the women themselves to apply for examination. A month or so after the confinement the woman has probably returned to her household duties or even to work, and she may not wish to be bothered with any more "doctoring" or with the trouble of making a journey to the hospital or clinic. She may feel quite well or else she may accept certain apparently minor trouble as part of the inevitable legacy of childbearing, hoping that a little more time will see complete recovery to normal.

The last difficulty is insufficient facilities for treatment. Many purely gynaecological conditions require a few days in hospital for such treatment as rest for subinvolution, cautery of cervix, and treatment for hæmorrhoids. Other patients need physical treatment at the hands of a masseuse or physical exercises for which the facilities are very few and difficult to get except for those who live in large towns.

### POST-NATAL EXAMINATION

It is usual to make a pelvic examination before the patient gets up to note the position of the uterus and condition of the perineum and lochia. But it is after a month or six weeks that the woman needs a complete overhaul.

The general scheme may take the following or some similar form :—

1. General condition and appearance. The patient is asked how she feels, if she is abnormally tired after effort, if she has backache, abdominal discomfort, hæmorrhoids, varicose veins, shortness of breath, difficulties in micturition, white discharge or bleeding, faults in bladder and rectum control, sleep, appetite, digestion and bowel action, the progress of lactation and the baby. Some women may make the general complaint of being over tired, run-down, and depressed. These people may show a mild anæmia, and muscular relaxation following too short a time in bed and early resumption of hard work. No one condition is emphasised. The state is the result of a mild degree of sub-normality of all visceral function. Almost every question is answered positively. The patient will admit to headaches, giddiness, flatulence, dyspepsia, and constipation. She is suffering from a "post-partum debility," which unless treated at once will remain as a chronic state of sub-health lasting perhaps for years. These are the women who

later say they "have never been the same since the baby was born."

The treatment consists chiefly of rest in bed for at least a fortnight and such other remedial measures as may be indicated by the chief symptoms. Later, physical exercises to tone the muscular system are an important feature.

2. Presence of anæmia. Hypochromic anæmia in pregnancy is a common condition which may be intensified by labour and carried over to the puerperium. Should the woman be inadequately nourished or overworked, the anæmia may persist in a chronic form, perhaps in a relatively mild degree, but as a cause of fatigue, depression, lack of enterprise and ability to cope with her normal household duties and the care of the child.

Inspection of the conjunctivæ is not sufficient to give real information except in pronounced cases. It is a simple matter to make routine estimations of the hæmoglobin percentage in all doubtful cases, and this should be done. A reduced percentage of 85 or below should be treated by iron in the usual way, but occasionally anæmia is more pronounced and is associated with other symptoms which suggest it is of the pernicious type. Such patients may have achlorhydria. They need further investigation and suitable treatment with liver, iron, hydrochloric acid and rest in bed in hospital, if this can be arranged. Insufficient attention has been devoted to anæmia in women. It is at the post-natal examination that anæmia resulting from childbearing can be detected. It should be treated before it becomes a chronic condition. This is particularly essential during the war-time conditions of feeding, when eggs are scarce, when green vegetables are not eaten by the working classes in sufficient amount (often due to the time of preparation and cost of cooking), and so long as there is general unpopularity of whole-meal or even 85% extraction bread.

Any woman who has a reduced hæmoglobin should have a red cell count made and colour index calculated. Not only should these patients be given iron and other appropriate treatment, but they should be most carefully advised on their diet and instructed in what to buy, cook and eat in order to give the maximum intake of iron. In the long run they will have to maintain their normal hæmoglobin level, not by taking iron preparations, but by eating the best iron-containing foods.

3. The muscular system. Many women suffer from muscular relaxation and general lack of muscular tone for months and even

years after labour. The chief evidence of this is sagging of the abdominal wall while standing, but there may also be lack of firmness of all the muscles such as those of buttocks and calves. Simple muscular exercises either cannot be done or only by great effort. Many women with a slack abdominal wall are unable to raise their lower limbs to the vertical while lying on the back, and during the effort may show much divarication of the recti. There is difficulty in doing other simple exercises which should give no trouble to a normal woman. Now visceral health cannot exist if the abdominal wall is loose and slack in the erect position. The later results of the toneless abdominal wall will be visceroptosis, dyspepsia, flatulence, constipation and many other symptoms based upon the atonic state. We do not suggest that a condition so deep seated in its pathology as visceroptosis is due simply to a toneless abdominal wall following the distension of pregnancy. There are other factors involved, including a mental state, often similarly atonic, and probably an endocrine factor acting upon the para-sympathetic. A first pregnancy may be followed by a long, perhaps permanent period in which the abdominal wall is slack and toneless, while on the other hand some women who have had many children manage to preserve a good abdominal contour. There is some factor deeply inherent in the individual which influences muscle tone, which confers on him or her their characteristic type. This has nothing to do with muscular development or strength. Women in whom the muscles tend to be soft, relaxed and easily fatigued, those without vigour of personality, those who wilt easily under a stress—such women are prone to develop after labour the muscular deficiencies we have described, particularly those of the abdominal wall.

While it is true that visceroptosis is based upon more than a relaxed abdominal wall, yet if the tone after labour is so poor as to allow proptosis, there is an additional factor contributing strongly to the development of visceroptosis. The muscle of the abdominal wall, therefore, is a most important structure in the early days after labour, and should be treated if necessary before a chronic toneless state becomes established. The treatment should be a suitable course of graduated exercises under instruction by a masseuse. Related to the condition of the abdominal wall, and muscular system generally, is posture. The atonic state will lead to bad posture on standing and walking. Correction of faulty posture will assist in any exercises which may be advised

as physical treatment. It is difficult to remember one's posture while walking, but the patient should be urged to do her utmost to remember to hold herself erect.

4. **Perineal and pelvic examination.** The usual inspection is made for unhealed lacerations, persistent lochia or leucorrhœal discharge. Palpation will determine the position and size of the uterus. These details constitute the whole of most post-natal examination as commonly performed and need not be described in detail. An important point which may be overlooked is the tonicity of the levator ani muscles and the degree of involution of the pelvic floor. There may have been no serious laceration and will not yet be any organic prolapse, but straining down may produce a general bulging of the whole pudendal and peri-anal area. In the centre of the bulging area the anus, with relaxed external sphincter, will form the apex of a convexity. On asking the patient to contract the levator ani muscles, there will be little power and capacity to pull up the peri-anal region and anterior wall of the vagina against the symphysis.

This condition may be described as perineal sub-involution, and it can occur in the absence of any laceration. It may be a part of a general lack of muscular tone, or it may be a local defect caused by too long stretching of the perinæum by the emerging head during delivery. The attempt to avoid perineal laceration by allowing the head to distend it for too long may produce the very condition which it was hoped to avoid, namely, prolapse. It is true that an organic prolapse may have been prevented in so far as a tear has been avoided, but the long and severe stretching of the levator ani and perineal tissues will have prepared the way for a functional prolapse. The more general adoption of prophylactic episiotomy during labour with slow emergence of the head would do much to abolish "functional" prolapse. If, in addition, the woman after a prolonged delivery of the head, gets up and resumes work too soon, the relaxed tissues do not have the opportunity afforded by rest to regain their tone. Intra-abdominal pressure and weight maintain the tension on the as yet sub-involutud muscles and fasciæ with the result that these structures become more or less permanently relaxed. A proptosis of the perinæum rather than prolapse follows, but in some ways it is a more difficult clinical problem than a frank organic prolapse. It causes as much discomfort and distress, while it is almost impossible to treat by the ordinarily successful surgical operation for prolapse.

Not enough attention is devoted to the functional forms of perineal proptosis and "pelvic visceroptosis." The treatment must be rest in bed for a fortnight or so, to take the weight off the stretched tissues, combined with faradism and perineal "exercises." These take the form of repeated voluntary contractions of the levator ani muscles. Anæmia is treated, the diet should be generous, straining due to constipation is prevented, while general massage and exercises of the whole body is stimulating and helpful.

Minor unhealed lesions of the cervix should be cauterised and deeper tears repaired after six months. The retroverted uterus should be replaced manually and maintained in position by a pessary worn for two months.

5. Varicose veins and hæmorrhoids may still be a complaint after four or five months. Treatment will depend on their condition, but should never be neglected considering the subsequent discomfort which may be caused.

6. Some women who have had an abnormal pregnancy, due for example, to toxæmia, nephritis, heart disease, tuberculosis, or any other complicating condition, need overhaul and special care in maintaining a treatment service for months after labour. At present many of these patients, perhaps on a lower grade of health than when pregnancy began, drift back to an unsheltered busy home life without any observation, advice or treatment.

7. The teeth should be subject to a mirror examination in view of the known tendency of the teeth to deteriorate during pregnancy. The majority of women will need dental treatment, and it is well that it should be at this particular time.

8. Sacro-iliac backache may indicate sub-involution of the pelvic joints. A mild low central backache is a common feature of post-natal complaints, but that due to the sacro-iliac joints is localised and there is tenderness over the joints. In any case of doubt, both the sacro-iliac joints and the symphysis should be examined by X-ray. If the films support the clinical suspicions, the patient must be rested in bed for three or four weeks with massage and later physical exercises. It is most important that this condition should not be allowed to become established as a cause of chronic pelvic pain.

9. Lactation progress needs inquiry, sometimes advice and treatment. Where the feeding is unsatisfactory and the patient is worried and debilitated it is much better to stop suckling at once.

## THE POST-NATAL CLINIC

A self-contained post-natal unit serving a large maternity department or borough should consist of something more than an examination room.

The suite should comprise a waiting room, lavatory, interviewing room and examination room with suitable number of cubicled couches. In addition there should be a small room where hæmoglobin estimation and urine examinations can be made, and a dental room where the patient's teeth can be examined and treated conservatively wherever possible.

As so many post-natal women need physical exercises and massage, it is essential that a modern suite should include a department where these exercises can regularly be given under supervision by a professional masseuse.

Lastly, a number of beds should be available in the adjoining hospital for post-natal patients, to which they can be admitted for necessary rest or other in-patient treatment.

## CHAPTER III

### BREECH DELIVERIES

SOME changes in the management of breech presentations and breech deliveries which have become more or less standard obstetric treatment during the course of the last few years call for brief notice.

Firstly, the question of diagnosis. It cannot too strongly be stressed that when a breech presentation is discovered antenatally the diagnosis is only half complete. It is essential that the question, "Are the legs extended?", should be answered. For if a breech with extended legs be discovered its management, both pre-natally and intra-natally, is different from that of a full breech.

What, then, are the points which will establish the diagnosis of "breech with extended legs"? In the first place the mere discovery of a breech presentation in a primigravida is suggestive. It is found that in women pregnant for the first time, over 50% of the infants presenting by the podalic extremity, have the legs extended. The next most important point is finding the half-breech well engaged in the pelvic brim weeks before labour is due. On this early descent of the pointed half-breech depend several of the other physical signs of the condition, viz. (1) the foetal heart being heard in the positions commonly associated with vertex presentations and not above the umbilicus. It is the full breech at thirty-six weeks or more of gestation which, sitting on top of the pelvic brim, manifests foetal heart sounds in this position. Cases of extended breech have the buttocks and consequently the foetal trunk sunk into the mother's pelvis in a manner which will obviously result in the heart sounds being audible at a low level on the maternal anterior addominal wall—generally well below the umbilicus. It follows that (2) the fundus of the uterus will be lower in the abdomen than would be expected for the duration of the gestation. For descent of the presenting part is naturally accompanied by descent of the fundus. Lastly, in these cases, free ballottement of the head at the fundus is often interfered with by the splinting action of the extended legs and the frequently associated extended attitude of the arms. At the same time the whole attitude of the foetus with the straight spine and firmly set head is sometimes described as "military" and may itself suggest the correct diagnosis.



Clinically, therefore, the experienced obstetrician should have no difficulty in recognising cases of breech presentation, and should find it almost equally simple to pick out those cases in which the legs are extended. The too frequent recourse to radiological examination in order to make a correct diagnosis of the presentation and attitude should be regarded as to some degree a confession of incompetence. Nevertheless, the correct thing is to have an X-ray examination made in every doubtful case. And it must here be admitted that in difficult cases when the abdominal wall is held rigidly or when the uterus is irritable, it is not unreasonable to be in doubt whether a given presentation is a breech with extended legs or a vertex. The reasons for this are that the pointed half-breech sunk in the pelvis feels not unlike a head, while the head at the fundus, not showing free ballotement, and having limbs near it may be difficult to distinguish from a breech. In such cases, therefore, X-ray investigation is desirable. Otherwise the doctor may find himself dealing with a patient in labour at full term with a large child which he had thought was presenting as a vertex, but which the dilating cervix now reveals as a breech with extended legs.

This may be a suitable moment to speculate on the part to be played by X-ray examination of the pregnant woman in years to come. As stated above, we now deprecate the too frequent recourse to radiology as undesirable, in that it hinders the development of clinical knowledge and experience. But it is probable that many will never acquire sufficient skill in palpation to be certain of their diagnoses, and will be forced to rely more and more on radiology. Also, that if radiological examination is not made, their errors in diagnosis, even forgivable ones, as, for example, the case of breech with extended legs simulating a vertex presentation as described above, may involve them in actions for damages. Gradually, therefore, it is possible that the routine X-ray examination of every pregnant woman will become general, just as has the routine radiological examination of every case of fracture.

### Version

The time in pregnancy when it is essential to recognise a breech presentation, with its possible associated complication of extension of the legs, is the thirty-second week. Prior to this, it is hardly necessary to trouble about the presentation—it is so variable. But at the thirty-second week it must be recognised.

so that time is given for the making of any necessary arrangements for version. Until recent years it has been customary not to do version on a full breech until the thirty-sixth week, since up to this time spontaneous rectification of the presentation is usual. But all would have been agreed that cases of breech with extended legs should be turned not later than the thirty-fourth week, since version in these cases is much more difficult.

In the last few years there has been an evident tendency to do versions earlier than the above times. In fact many turn the foetus whenever any malpresentation is recognised, however early in the pregnancy this may be. In 1939, Abercrombie (4) read a short paper entitled the "Elimination of the Breech Presentation from Private Practice." This should be the aim and object of all good obstetricians. In that paper, not only was this principle enunciated but also the value of early version was indicated. It is now generally recognised that by doing version early, the actual performance is facilitated; but since version, even gently performed, carries some risk of separation of the placenta, onset of premature labour, rupture of the membranes with or without prolapse of the cord, and even rupture of the uterus, the performance of any unnecessary version is still criticised by a few obstetricians as being not without risk. But these risks will be seen to be remote—so remote that if the version is capable of performance without an anæsthetic they can be disregarded. And even when anæsthesia has to be employed such risks are really almost negligible provided that undue violence is not employed.

There can be very little doubt nowadays that even if it be accepted that there are some dangers, the risks of version performed at the right time are adequately counterbalanced by greater safety to the mother and far greater safety to the child. And if version cannot be performed without an anæsthetic few would be found to object to an attempt under full anæsthesia. But any approach to violence must be avoided; careful observation should be kept on the condition of the foetal heart, and relaxation must be good before the attempt is commenced. In other words, gas and oxygen is not the anæsthetic for version.

Here we may consider some figures from different obstetric hospitals which give an indication of the prospects of success when prophylactic external version is attempted, the dangers of this manoeuvre and how the risks contrast with those of delivery as a breech.

In the Obstetric Unit of University College Hospital, White and

Flew [quoted by F. J. Browne (2)] found that in 298 cases version was successful in 76% of patients in the primigravid group and in 94% of the multiparous group. They found that the risk of premature labour was "negligible" when no anæsthetic was used but premature labour occurred in 8 out of 40 versions performed under anæsthesia after the thirty-seventh week of pregnancy. This last point seems important to us. For it will be found as a clinical fact that version relatively early in pregnancy, say, at the thirty-second or thirty-fourth week is *not* followed by the premature onset of labour even when anæsthesia has been required for its performance. But version near full term carries a great chance of this happening.

In the University College Hospital series it is further noted that among 201 versions performed without anæsthesia there was no instance of placental separation and consequent hæmorrhage occurring as the result of the manipulation. But bleeding was provoked in 6 out of 92 patients who were anæsthetised.

We will next consider the findings at another hospital, and the following figures are extracted from Queen Charlotte's Hospital Reports:—

## 1938

## CASES OF EXTERNAL VERSION

Primigravidæ :	No anæsthesia.	Success	23.	2 subsequent dead births.
		Failure	1.	Delivered as breech.
	With anæsthesia.	Success	18.	No subsequent dead births.
		Failure	4.	Delivered as breech.
Multiparæ :	No anæsthesia.	Success	34.	2 subsequent dead births.
		Failure	0.	
	With anæsthesia.	Success	5.	1 subsequent dead birth.
		Failure	2.	Both delivered as breech.
Summary :		87 versions tried. Success in 80 cases but followed by 5 cases of dead birth.		

## 1939

## CASES OF EXTERNAL VERSION

Primigravidæ :	No anæsthetic.	Success	24.	1 subsequent dead birth.
		Failure	1.	
	With anæsthetic.	Success	21.	1 subsequent dead birth.
		Failure	14.	All delivered as breeches.
Multiparæ :	No anæsthetic.	Success	44.	1 subsequent dead birth.
		Failure	0.	
	With anæsthetic.	Success	4.	No dead birth.
		Failure	4.	
Summary :		112 versions tried. Success in 93 but followed by 3 subsequent dead births.		

The explanation of the high proportion of failures among cases with anæsthesia is clearly that this was selected only for the more difficult versions.

If the two years be combined we get the following table :—

Total number of versions attempted . . . . .	190
Total number of successes . . . . .	173 = 80.4%.
Total number of subsequent dead births following version . . . . .	8
Percentage dead births after successful cases of version . . . . .	4.62

It would thus appear that version should be successful in nearly 90% of the cases in which it is attempted and that the probability of success is greater in the case of multiparæ than of primigravidaë. Furthermore, that up to 5% of version cases are delivered of a dead-born fœtus. From this we must perhaps assume that 1 to 2% of the dead births must be attributable in some way to the act of version and that the remainder are the unavoidable fœtal risks of being born.

How does this compare with the fœtal results of breech delivery? Let us continue with figures extracted from the Queen Charlotte's Hospital Reports.

### Fœtal Mortality in Breech Delivery

In the 1937 report it is seen that there were 56 breech deliveries with no maternal deaths. Among the 56 babies 11 were still-born and 5 died soon after birth, thus making the fœtal and neonatal still-birth rate 30.4%. But this hardly represents the figure we want to know. What the ordinary obstetrician may be imagined to ask himself is the question—out of 100 breech deliveries without complications, how many babies must I expect inevitably to lose as the result of that delivery?

In attempting to answer that question we take the above 16 dead babies and exclude 8 cases (1 fœtal abnormality, 3 premature, 4 macerated), for which no obstetrician can take responsibility. This reduces the fœtal and neo-natal death rate to 14.3%. Even this does not quite complete the investigations, for a little further on we find among the cases of "complicated breech deliveries, 1 case of primary inertia, 1 case of uterine exhaustion, 1 case of prolapsed cord and 1 case of contraction ring." These cases must be included to get a fair answer to our question. And among these cases are 3 still-births. The corrected figure would thus seem to be 11 still-births and neonatal deaths among 60 breech deliveries—in other words, 18.3%.

In the 1938 report we find details of 52 uncomplicated breech deliveries—88 primigravidaë and 14 multiparæ. Five babies

were still-born and 3 died. But of the still-borns, 2 were macerated and all the "died" were of thirty-six weeks or less maturity. Only 3 still-births thus emerge as quite unavoidable but to these we have to add 4 cases from the complicated breech delivery tables (*i.e.*, 2 cases of prolapsed cord; 1 case of disproportion; 1 case of contraction ring) with 2 still-births. The average doctors' cases would thus total 56, among which he loses 5 babies or 9%.

The figure for 1939 is close to that for 1937 but the time has come to study the results from other centres.

The Glasgow Royal Maternity Hospital in 1937 reports 297 breech cases, 144 primigravidae and 153 multiparæ. There were 74 still-births, from which we can exclude in all 29 cases such as hydrocephalus, ante-partum hæmorrhage and toxæmia, leaving 45 which can be regarded as the average obstetrician's inevitable loss and which in still-birth percentage figures is 15.1. The infantile deaths were attributable to prematurity or other unavoidable factors and are therefore excluded.

A similar analysis of the 1938 figures from the same hospital shows 71 still-births among 349 cases. Thirty-five still-births being due to foetal abnormalities; ante-partum hæmorrhage toxæmia can be excluded, thus leaving 36 still-births or 10.3% as the foetal still-birth rate for average breech deliveries which the average obstetrician would have to face. Curiously enough the "unavoidable" still-birth rate among 358 cases at the Glasgow Royal Maternity Hospital in their 1939 report again works out at 10.3%.

It would therefore appear that somewhere in the region of 12% must be accepted as the still-birth rate which must be expected among babies delivered as breeches by the average doctor, and that to this must be added a certain proportion—perhaps 5%—of neo-natal foetal deaths directly attributable to the breech delivery. There can therefore be no argument, as to the advisability of version. It is uncontroversial that the foetal results after that manipulation are vastly better than are those for breech deliveries. This remains true in general, even if certain expert obstetricians can produce a series of breech deliveries which, in their skilled hands, yield exceptionally good foetal results.

Despite attempts at version even under anæsthesia, there will remain cases in which the malpresentation cannot be rectified. This is more usual in cases of extended breech, but may occur in complete breech presentations. In these latter cases little need be

said here about the management of labour up to the time for delivery of the head. But for this there is a recent change of practice. It is usual now to avoid "jaw flexion and shoulder traction" if possible and to try first the method described by Burns (3), in which, the patient being on her back, the child's body is allowed to hang vertically from the vulva as soon as the arms and shoulders are delivered. Next, delivery is secured by a combination of suprapubic pressure with the left hand, while the right hand clasps the child's ankles, keeps the child's trunk gently on tension and carries the child's feet and trunk upwards in a semi-circle towards the mother's abdomen.

In cases of breech with extended legs, however, a considerable change has occurred in the generally accepted management. In the first place, if an elderly primigravida is found to have an extended breech presentation, some obstetricians would avoid the foetal risks attendant on version or delivery as a breech, by performing Cæsarean section at term. But many would prefer at least to attempt version and even go so far as to try the manoeuvre under anæsthesia—Cæsarean section being reserved for those cases in which version fails.

But in younger women there is no question of Cæsarean section except for cases of gross disproportion. The extended breech presentation having been diagnosed, external cephalic version is attempted at the thirty-fourth week, the thirty-second week or even earlier. If this fails without anæsthesia, then the woman is anæsthetised to the surgical degree with, preferably, a chloroform-ether mixture or possibly one of the intra-venous anæsthetics. She is then placed in the Trendelenberg position so that gravity will help to disengage the breech from the pelvis and a further attempt at version made. If necessary, an assistant can help to push the presenting part out of the pelvis with two fingers in the vagina.

In all cases in which version fails the subsequent management must be guided by the recent teaching (4) that, given a good sized pelvis, a breech with extended legs can be delivered with the legs extended. The old practice of bringing down the anterior leg as a routine, when the cervix is sufficiently dilated to permit of this, is now generally abandoned. But the point of paramount importance is that there must be a sufficiency of room in the pelvis. The subsequent treatment then can be epitomised thus: If there is plenty of room, allow the case to come into labour naturally at term and deliver as a breech with the legs extended; if there is not plenty

of room, many obstetricians choose to induce premature labour at or shortly after the thirty-sixth week so as to secure the facile delivery of a small baby through a pelvis which was not considered adequate easily to pass the larger child of a full-term pregnancy. With regard to the method of induction to be employed, we recommend separating the membranes from the lower segment of the uterus by means of a finger passed through the cervix after dilatation if necessary, the patient of course being under an anæsthetic. Then a long rubber bougie, like a solid stomach tube, is introduced. This coils up in a spiral manner in the lower segment and is removed when labour is well in progress. This method of induction would appear generally to be preferred to artificial rupture of the membranes for cases with this malpresentation. For should labour not commence as the result of rupturing the membranes it is difficult to know what next should be done.

The actual labour, induced or at full term, is allowed to proceed naturally until the breech is distending the perineum. At this point episiotomy should be performed in all cases. This facilitates delivery and is probably a safety factor with regard to the child. A well-known maternal risk of breech delivery is extensive tearing of the perineum. The performance of episiotomy replaces with a clean cut the jagged tear of the spontaneous laceration. But the clean cut must be made to pass laterally to the anal sphincter.

Once the perineal resistance is thus eliminated, further advance of the half-breech occurs and in time the popliteal spaces of the extended legs reach the vulva. By pressing in the hollow of the knees it is now simple to cause the legs to flex and to bring about their delivery. The ordinary routine management of a breech birth is now followed, a loop of cord is brought down, etc., and, if, as is probable, the routine examination reveals extended arms, they are brought down—first the posterior one—by the standard manœuvre. The delivery of the head is secured by the method described earlier in this chapter.

There remains one further case for discussion, and that is the one in which a breech with extended legs was mistaken for a vertex. In these cases it is only when the patient is in labour and the cervix is dilating that the error is discovered. In the subsequent management of the case the considerations outlined above still guide us. If it is considered that though at full term the child is small enough and the pelvis large enough for delivery with the legs extended to occur with reasonable ease, then the case is left so to progress. But if it is considered that the amount of

room is insufficient, impaction of the half-breech at the outlet is to be feared. This, then, is the case—and the only case—in which it is advisable to anæsthetise the woman as soon as the cervix is sufficiently dilated to permit intra-uterine manœuvres, and to bring down the anterior leg. At the same time it may be found feasible to move the arms from their possibly extended position and to fold them under the chin of the fœtus. Some obstetricians would also bring down the posterior leg, but it is really only the anterior one which must be brought down to facilitate delivery.

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## CHAPTER IV

### PYELITIS

URINARY infections in pregnancy are important on account of their great frequency and liability to cause chronic ill-health. Occasionally, the infection may be so acute as to endanger life, both of the mother and foetus, and, until the recent work of Rosenheim, Kenny and others had shown the first methods of specific treatment, it was often an intractable disease which defied all attempts to eradicate it. Recent advances, however, in our knowledge of physiology, pathology and treatment have quite altered our conception of the disease and rendered it possible for us to cure the large majority of all cases, if not during pregnancy, at least during the puerperium.

The clinical varieties vary from a "cold" condition of bacilluria without any obvious symptoms for long periods, to an extremely acute infection which involves not only the ureter and renal pelvis but also the renal tubules and causes a long period of high fever and illness.

Diagnosis is usually easy if the possibility of urinary infection is borne in mind, but mistakes are often made because the urine is not examined bacteriologically. As a cause of vague pain during pregnancy, pyelitis may easily be unsuspected unless a pyelogram is made; while the acute mild febrile form may be mistaken for acute appendicitis, or uterine infection during the puerperium. Perhaps the chief gain that has followed the recent research is not so much the treatment of the acute attack as the possibility of preventing a long-standing chronic bacilluria, which undermined health and caused repeated attacks of minor febrile illness. There have been two main lines of attack on pyelitis. Firstly, the work of Stoekel (1925), Schumacher (1928), Gremme (1) (1931), Traut (2) (1937), and particularly of Baird (3) (1934-35), which has shown the changes in the ureter during pregnancy, and the variations of secretion and ureteric pressure caused by obstruction and diminution of tone in unstriated muscle. Secondly, the original observations of Clark and Helmholz (4) on the vulnerability of *Bacillus coli* in urines of varied pH led to the specific treatment by the ketogenic diet, whereby the pH of the urine was reduced below 5.5. Later, Fuller (5), at Queen Charlotte's Hospital, examined the chemical condition of the

bactericidal urine produced by the ketogenic diet. This led directly to the work of Rosenheim (6) on mandelic acid, an agent which has an almost specific action on *B. coli* bacilluria and at the time, entirely altered both the treatment and the prognosis. More recently still the value of sulphanilamide has been confirmed by universal experience.

The story of the attack on pyelitis is a good example of the effect of combined laboratory and clinical research in producing exact knowledge of the pathology and treatment. From an almost empirical beginning it has progressed to a degree which is now almost specific.

### Incidence and Bacteriology

Large series of pregnant women have been examined for bacilluria, irrespective of the presence of symptoms. Traut found that in 15,000 consecutive deliveries 2.02% of the women had pyelitis, while other authors have reported the incidence of bacilluria as high as 15% of all pregnant women. Baird, by very careful methods, found that 7.0% of all normal pregnant women in whom the urine is sterile at the beginning of pregnancy, develop urinary infection before delivery; also, that though clinical pyelitis is a common disease, yet simple bacilluria is a much more frequent condition. This is not only true of pregnancy but also of the puerperium in which urinary infections are extremely common.

In ordinary clinical work it is usual to make a culture of the deposit of the centrifugalised urine in broth or on simple agar. This is a rough-and-ready method of obtaining a general idea of the bacterial condition of the urine, but it gives little idea of the number of organisms, the finer distinction between varieties, or the identification of a contaminant. A rich growth of *Bacillus coli* indicates an infected urine, while a few varied colonies, usually including *Staphylococcus albus*, strongly suggest a contaminated specimen. While the identification of the various members of the colon group is unnecessary for ordinary work yet it is of considerable importance to have a report on the number of microbes per cubic centimetre of urine for the purpose of watching the progress of treatment; and where some less common microbe has been isolated, such as *B. proteus*, it is necessary to know whether it is the infecting agent or a contamination. When there is either a heavy growth or a completely sterile culture the simple method of microscopic examination of the centrifugalised deposit and its

culture on an agar slope is sufficient to make a diagnosis, but in the lesser, or unusual infections, these methods are not adequate.

The following is a useful technique: the urine should be collected by catheter, with careful precautions, in the morning and examined within two hours to obviate the multiplication of organisms in the waiting specimen.

(a) Examine a fresh drop by the high power to note the presence of organisms or pus cells.

In all cases of pyelitis, both pus cells and organisms can be seen in the fresh drop. An idea of the severity of the infection can be gained by counting the number of both cells and microbes.

(b) Cultures are made from the centrifugalised deposit on agar, broth or McConkey media.

In the case of light infections, the organisms may be missed unless cultures are made from the centrifugalised deposit. while in heavy infections this culture may yield so thick a growth that identification of separate varieties of colonies will be impossible. In the latter condition the plates resulting from culture of the non-centrifugalised urine will grow more scattered and easily recognisable colonies.

(c) Examination of the centrifugalised deposit after Gram-staining for pus cells and organisms.

The significance of the presence and numbers of pus cells is the information they give on the stage of the disease. During the acute stage they will be present in large numbers and be roughly proportional to the severity of the attack, but as the disease becomes more chronic the number of pus cells will diminish and may almost disappear. In the final chronic stage the patient is left with little more than a bacilluria.

Employing the technique described above, Baird found that in 7.7% of cases in which no infection could be found by examination of the fresh drop the culture was positive, yielding the *Staphylococcus albus*. The inference is that the growth was a contamination and of no clinical significance. Similar results were noted when the deposit, after centrifuging, was inspected and cultured. On the other hand, in 16.6% of cases, the culture gave a negative result when the centrifugalised film showed organisms. The failure to grow on culture, in this group, is due to the organisms being dead.

In all cases of frank pyelitis microbes were found in the fresh drop; in a group of doubtful cases they were found in 72.7%, and in the group of apparently normal women. 36%. If, there-

fore, by the examination of the fresh drop after the first day or two, no organisms can be found, the woman is free from suspicion of urinary infection. Further, if a few pus cells are present in the fresh drop in conjunction with a negative culture, the patient may also be regarded as free from infection (Dodds (8) )

Dodds also states that, even if a few pus cells are discovered with organisms other than colon bacteria, they are of no significance. But care must be taken in interpreting the findings of examination of the fresh drop, for many bacteria with few cells usually indicate the passing of the acute to the chronic phase, and not the beginning of the acute stage.

### Incidence of Urinary Infection during the Puerperium

There is a higher rate of urinary infection during the puerperium than is commonly believed. Whenever a patient develops pyrexia, the first attention is rightly given to the uterus and the urine may be forgotten; but if the urine is carefully examined in all cases of pyrexia, about 10% will be found to have an infection. In many of these patients the bacilluria is of secondary importance to the major infection, such as cellulitis or septicæmia, but if all such conditions are excluded the incidence of bacilluria alone as a cause of puerperal pyrexia is nearly 10%.

The infection may arise *de novo* during the second week, or it may be a continuation of pyelitis of pregnancy. Of the first group it is found that where the urine is sterile before delivery, there is a proportion of 5% of patients who show heavy infection on the eighth day after normal delivery and 25% after complicated delivery (Baird). There is thus a very distinct association between labour and subsequent bacilluria. But of all cases of primary puerperal urinary infection there is only about one in ten which has pyrexia, or any other symptom, and these usually develop during the second week.

In the second group the pre-existing infection during pregnancy is either persistent through labour into the puerperium, or it exacerbates during the first week. Antecedent infection is a much more common cause of pyrexia than is pyelitis arising for the first time during the puerperium.

Of ætiological importance in the production of puerperal pyelitis is *B. coli* infection of the blood stream at, or just after, labour. It has been claimed by some writers that as many as 5% of all women have a bacteriæmia during the first hour after delivery, which rapidly disappears in normal cases. But

Baird has found a transient septicæmia in only 3·5%, of which more than half were due to *B. coli*.

The microbe is probably derived from the bowel in most cases, indirectly by passage over the perineum and into the vagina, but it is also possible for a pre-existing pyelitis to be a source of the infection.

Where urinary infection is found during the first three days of the puerperium, it may be due to a mild, even clinically unrecognisable *B. coli* septicæmia or a continuation of a pre-existing bacilluria of pregnancy. The late onset of pyelitis—primary puerperal pyelitis—has a different ætiology. A late *B. coli* septicæmia is much less common than that which is liable to occur immediately after labour and can account for only a very small number, but during the first two weeks after delivery we find in the atony of the bladder a new factor predisposing to infection. Whatever may be the cause there is a relaxation of the bladder which allows a painless capacity of as much as 40 to 50 oz., and, very commonly, a residual urine remains every time urine is passed voluntarily. Unless the catheter is passed daily, preferably at night, the bladder urine is very liable to be infected without necessarily producing a clinical cystitis. From the bladder, infection may pass into the ureters, especially the right, which is more atonic than the left, and so produce pyelitis.

It has been shown by X-ray photographs after filling the puerperal bladder with 6% sodium iodide, that there is little or no tendency towards reflux from the bladder to the ureter unless the bladder tone is fairly good. But though actual fluid reflux is uncommon, infection of the bladder is almost certainly conveyed to the upper reaches of the tract by the peri-ureteric lymphatics.

### The Infecting Organism

All writers agree that the great majority of all cases of pyelitis of pregnancy and many of the puerperium, are due to a member of the colon group. Dodds found that of 793 unselected patients during pregnancy, labour and the puerperium, 6·4% (51 patients) yielded some variety of colon bacillus, and 4·9% (43 patients) yielded *Staphylococcus albus*, occasionally *Staphylococcus aureus*, or a non-hæmolytic streptococcus.

In acute cases of pyelitis the organism is nearly always *Bacillus coli* (about 95% provided there is no calculus, tubercle or chronic gonorrhœa); but in the chronic cases *Bacillus coli* may be found

in conjunction with other microbes. Rarely there may be a pure infection by a pyogenic coccus. The varieties of the colon group described by Baird are as follows :

Organism	No. of Cases	Per cent. of V. acute cases.
<i>B. coli communior</i> . . . .	84	29.4
<i>B. acidi lactici</i> . . . .	36	25
<i>B. coli communis</i> . . . .	35	20
<i>B. aerogenes</i> . . . .	19	42
<i>B. neapolitanus</i> . . . .		
<i>B. coli anaerogenes</i> . . . .	14	14.3
Non-lactose fermenters . . . .	10	10

With the exception of the non-dulcitate fermenters there was little difference in the severity of illness between any of the varieties of organisms and, in general, the hæmolytic strains did not produce a higher percentage of serious illness than the non-hæmolytic strains. In recent and acute cases the usual variety is one of the first three given above, *i.e.*, one of the common forms of *B. coli*, but as the disease becomes chronic other members of the group may appear.

Bacteriological investigations have shown, therefore, that the finer differentiation of strains is unnecessary for ordinary clinical work unless possibly there are complicating foci of infection in other parts of the body; but even here it is unusual for any relation to be discovered between a septic focus elsewhere and pyelitis. Neither diagnosis nor prognosis is dependent upon the ultimate identification of the variety of the coliform organism, but the microbe must be defined when a urine is found which contains much pus, and the culture yields either a mild coli-pyogenic infection, or very little growth. In these cases further search must be made for tubercle or calculi. If, however, it is certain that neither tubercle nor calculus is present in a case which yields nothing but a small growth of *Staphylococcus albus* or non-hæmolytic streptococcus, these latter may be considered as contaminants.

During the puerperium, pure *B. coli* infections form a smaller proportion of urinary infections. Baird states that in heavy infections *B. coli* was found in only 57% of cases and in 23% of

the light infections. The other microbes commonly found in the puerperium are *Staphylococcus albus* and some strains of non-hæmolytic streptococci. The alteration in the flora, as compared with ante-natal pyelitis, is probably associated with the atonic bladder and residual urine after delivery forming a new element in the ætiology.

### The Ureter in Pregnancy

In order to understand the changes which may take place in the ureter during pregnancy and the puerperium it is necessary to recall certain points of anatomy and also, perhaps, of endocrinology.

The abdominal part is 14 cm. long and terminates at the brim of the pelvis, where it passes over the iliac vessels. It lies on the psoas fascia and directly beneath the peritoneum, under which it can freely move in a lateral direction. At the pelvic brim the ureters are projected forward by the iliac arteries, especially on the right side, but on the left the pelvic colon and its mesentery afford some protection against any pressure exerted by the growing uterus.

During their pelvic course the ureters run beneath the posterior layer of the broad ligament under the uterine artery and forward to the bladder. The histology of the pelvic portion differs from that of the abdominal in that the muscle layers are more strongly developed, and at the terminal parts a specially dense coating of connective tissue—ureteric sheath—is found after the fifth month. This local hypertrophy was erroneously thought to be a factor in producing stasis and dilatation.

The lymphatic channels are probably an important element in the ætiology of pyelitis. It is believed that they pass directly upwards from the base of the bladder, where they are connected with those of the cervix, in the submucous and connective tissue walls of the ureter to the lymphatic meshwork of the renal pelvis.

The peristaltic waves of the ureter vary considerably in rhythm and rate. They are largely dependent upon the rate of excretion by the kidney and the pressure of urine in the ureter—the greater the pressure, up to a point, the more frequent are the contractions. A peristaltic wave may not pass the whole length of the ureter from the renal pelvis to the bladder, nor need every wave begin at the pelvis. Reverse peristalsis may occur, as can be shown by the shadow of an opaque fluid introduced into the lower end of the ureter reaching the kidney within a few minutes.

Complete ligation of the ureter stops all peristalsis, but partial

ligation causes increased peristalsis and a rapid elongation of the part above the obstruction, with the formation of kinks. Obstruction due to partial ligation also causes muscular hypertrophy and little or no dilation, the exact opposite of the condition in pregnancy, where there is dilatation and no hypertrophy except at the terminal inch of the ureter.

The physiology of the ureter has been investigated in man by Schumacher, Gremme and Baird amongst many others. X-ray examination of the ureters after injecting an opaque fluid shows that the renal pelvis alternates from diastole, during which it is receiving the excretion of the renal calyces, to systole, by which it empties its contents into the ureter in about ten minutes. The discharged urine forms a spindle-shaped enlargement of the ureter which travels down to the bladder in about five seconds or less. X-ray examination of the ureters after injection of uroselectan-B gives results which are likely to be more in accordance with those of physiological reality, inasmuch as the ureter is not abnormally irritated by the introduction of a catheter and sodium iodide. Where there is no ureteric stasis, however, it may be difficult to get any good photographs because the opaque urine is passed too quickly along the ureter. In pregnancy there is usually sufficient retention in the ureter to yield suitable films.

Trattner, Wright and Barlow (9), and Baird have used and described an apparatus (the hydrophorograph) whereby the tone of the ureter may accurately be measured. Much of our knowledge of the behaviour of the ureter under various conditions has been derived from investigation by this instrument.

The action of drugs on the uterus in pregnancy is of interest. Until about the thirty-eighth week the uterus is passive, that is it has capacity for relaxation and distension, while the tone and contractile power are minimal. During this period the oxytocic principle of the posterior pituitary lobe is absent. Just before term the uterus becomes sensitised to the action of this substance (pitocin), but after the first few days of the puerperium the uterus again becomes insensitive.

Running parallel to these uterine changes we find, as we shall describe later in greater detail, that the tone of the ureter varies. The action of histamine on the uterus in labour is to cause a rapid, strong but short-lived series of contractions (Bourne and Burn (10)), while Gruber (11) finds that dilute histamine also causes an increase in ureteric peristalsis. Our present knowledge suggests that uterine activity in pregnancy and labour is indirectly



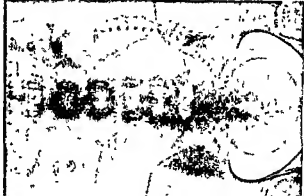


Fig. 4. Pyelogram of a case of acute pyelitis in pregnancy, showing delayed excretion on right side.

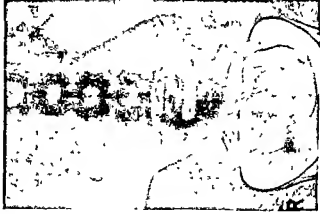


Fig. 5. Pyelogram from same case as Fig. 2, taken twenty minutes later, showing appearance of the dye on the right side, and associated changes in the right calyces. Note the kinking and dilatation of the left ureter.



Fig. 6. Pyelogram of case of pyelitis, showing faint outline of hydronephrotic changes and kinking and dilatation of ureter on right side. Note contrast with normal left side.

based upon the availability of œstrone in the body, and it is probable that ureteric tone is also governed by the same endocrine mechanism.

### Post-mortem Examination

The most frequent and striking change to be observed is dilatation, chiefly of the right ureter. This is also true in toxæmia, and the most extreme degree of dilatation that we have seen, occurred in a woman dead of eclampsia. Baird finds that dilatation was noticed on the right side in 69% and left side, in 40.6% of primigravida, and in 25.7% and 17.3% right and left, respectively, in multipara. The dilatation begins from the third month and is well established by the middle of pregnancy. The pelvic brim is a nodal point of importance, for in most cases the dilatation involves only the abdominal portion of the ureter, suggesting that it suffers a real pressure at this level. Where the pelvic part is dilated, the obstruction probably lies in the excessive hypertrophy of the ureteric sheath around the terminal portion. Many pyelograms show kinks of the right ureter below the renal pelvis and immediately above the pelvic brim. They are found post-mortem to be organic structures having some depositions of fibrous tissue which maintain the deformity. If pyelitis has been acute and prolonged, the fibrous tissue may be sufficient to ensure permanent distortion, but normally, where no infection has been present, they disappear some weeks after delivery.

A ureteric kink is not obstructive to the passage of fluid, though it may interfere with the smooth passage of the ureteric wave, but if particulate pus engages in a kink it may cause obstruction and pain of the degree of renal colic.

Ureteric kinks, therefore, may be important if infection is present as a cause of obstruction to purulent urine, tending to increase the retention and infection, and also to produce severe pain (see Figs. 2, 3, and 4).

All the evidence supports the view that there is direct pressure of the gravid uterus on the ureter, chiefly the right, as it crosses the pelvic brim. Pressure can be demonstrated post-mortem on women who have died undelivered; it can be increased by direct pressure on the abdominal wall, and is more likely to occur in primigravida with firm abdominal walls or in cases of increased intra-abdominal pressure from any cause. It is relieved by relaxation of the psoas when the thigh is drawn up, by lying on the left side, by passing a

catheter to a point above the pelvic brim, and by evacuation of the uterus. But mild or moderate pressure alone is insufficient to cause dilatation. A moderate rise of pressure in the ureter stimulates a stronger and faster peristalsis, and in gynecological conditions where the ureter may be compressed just as much as by the pregnant uterus, dilatation may occur, but is much less common. In addition to pressure there is the change peculiar to pregnancy—atony, which, when combined with obstruction to the outflow at the brim, allows dilatation, elongation, kinking, stasis and infection. In this combination and sequence we can see the reason for the genesis and frequency of pyelitis of pregnancy.

### Ureteric Stasis

As we have described, the result of pressure and atony is stasis of the urine between the kidney and the pelvic brim. The upper ureter forms a kind of reservoir into which urine is poured at the top, and from which it escapes past the obstruction at the brim into the pelvic portion of the ureter and bladder.

The first to investigate the condition of the upper ureter in pregnancy by pyelography after injection of uroselectan was Schumacher (12). Gremme repeated and enlarged his work and showed by a series of X-ray photographs both dilatation of the upper ureters and stasis of the urine. The delay in output was not due to loss of kidney function (since he chose for investigation those women who had normal kidneys) but due to changes in the ureter. All the dye was excreted in three hours. From the second to the fourth month of pregnancy no changes were observed. From the fifth to the tenth months there was always noted a marked dilatation of the upper ureter, in 25 cases on both sides, in 6 cases on the right only, and in 8 cases on the left only. By chromocystoscopic examination Gremme found 25 cases of delay from ten to forty minutes, out of 34 examined. Of these the great majority were on the right side, and only 3 on the left side.

But correlating the two methods of examination, he showed that there was no necessary association between dilatation (or atony) and stasis. The delay of the ureteric stream is part of an entirely altered, but normal, secretory mechanism, found only in pregnancy and the puerperium. One of the results, as witnessed by the cystoscope, is much longer intervals between the "puffs" of urine and the greater volume of each individual "puff." In passing we may refer to some important practical points in mcystoscopic examination. After injection of 5 c.c. of

0.4% of indigo-carmin; dye should be clearly visible in the ureteric efflux within five minutes. If the renal function is normal any delay is due to the upper ureter being dilated to form a kind of secondary bladder or reservoir. Normally, the ureteric peristalsis ejects urine into the bladder about six times a minute, but during the latter half of pregnancy there may be an interval of from five to fifteen minutes between the "puffs." One of the noteworthy features is the irregularity both in frequency and quantity of the "ejects."

The peristalsis may obviously be strong and vigorous, or the ureteric orifice may appear to be actually "incontinent," so that urine can be observed leaking continuously into the bladder. Great delay and "leakage" generally mean atony and are found in cases of acute pyelitis. A good demonstration of the reservoir-like condition of the right ureter is provided by the effect of massage over the right ureter about half an hour after indigo-carmin has been injected. If during a long interval between the "puffs" the ureter be massaged downwards a continuous flow can be observed through the orifice until the ureter has been emptied. During chromocystoscopy it is essential to watch the orifice for a considerable time to be sure of the conditions, owing to the great irregularity of efflux. The gradual passage of a ureteric catheter will empty the various parts of the tract. For example, there may be a gush of urine immediately after it enters the ureter, or not until it has passed above the pelvic brim. At this position of the catheter eye it drains the usual ureteric reservoir, from which the gush is obtained—up to as much as 25 c.c. within three minutes.

The catheter will also feel the kinks; in fact, there may be resistance at the level of the pelvic brim, and it may be impossible to pass it above the upper kink into the pelvis of the kidney.

### Pyelography

X-ray examination of the ureter may be done either after intravenous injection of 20 c.c. of uroselectan B or by injection of an opaque fluid (12% sodium iodide) through an ureteric catheter. The former is easier, safer and more "physiological." Rapid, even normal action of the renal pelvis and ureter may not allow enough of the dyed urine to occupy all the tract at any one moment to give a satisfactory shadow, but during pregnancy the usual stasis ensures that at least the upper two-thirds of the

ureter contains a large amount of urine for comparatively long intervals.

The pyelogram will show us the time of appearance of the shadow in the renal calyces, the site of the ureteric dilatation, and the presence of kinks and displacement of the ureters. It will also show the existence of the compression of the ureter, if, during the phase of dilatation, say at the sixth month, the patient is turned over to the left side. By the alteration of position the uterus falls away from the brim of the pelvis and relieves the pressure on the ureter, which quickly empties itself.

Baird sums up the changes in the ureter during pregnancy as learnt by the various methods of investigation, as follows :

"There are considerable variations in the changes both in different primigravidae, on the two sides, at different times in pregnancy, and in women of different parity. In general, the changes are most marked in primigravidae and on the right side, and least marked in multiparae and in the left ureter. The series of changes in an average primigravida, in the right ureter, is that at the second month there is some delay in excretion and irregular action of the ureter due to reduced tone. During the third month there is a recovery in tone and increased rate of excretion. During the fourth month the tone is again diminished, particularly on the right side, and becomes progressively more obvious throughout the fifth month until the sixth. From the sixth month till term there is often a recovery of tone with improvement in the rate of excretion which, on the left side, may become quite normal just before labour. Ureteric peristalsis is regular during the later weeks, but despite this the right ureter may remain dilated and cause retention of urine within its dilated portion."

In a few cases the dilatation may be associated with spasm of the part immediately below the renal pelvis or above the bladder, but as a rule there are no symptoms unless infection occurs. The condition of stagnation in the dilated portion strongly favours infection, and it is remarkable not that infection occurs as often as it does but as infrequently. After delivery the dilatation disappears because pressure against the brim of the pelvis is no longer present, but after three or four days the tone again diminishes considerably, reaching its maximum during the second week. Ureteric tone gradually returns to normal during the following month. This puerperal stasis may account for the not uncommon incidence of pyelitis during the second week of the puerperium. The degree of atony after labour is proportional to that which obtained during pregnancy, and this applies also to the rapidity with which normal conditions are established.

### Diagnosis

a rule there is no difficulty in diagnosis of a case of pyelitis of pregnancy. The combination of pain in the right side, fever, urine with pus and *Bacillus coli* in the urine establish the diagnosis. But there may be difficulty where there is pain only. Examination of the urine during the first day or two may reveal no pus or bacilli, and in the absence of this critical test the renal tract may be overlooked. The site of the pain is often the right iliac fossa, or, even more commonly, over the right ureter immediately above the brim of the pelvis. It is less frequent and less marked in the renal region, which is a reason for failure to recognize that the pain arises in the renal tract, and for a mistaken diagnosis of appendicitis.

The site of maximum tenderness corresponds to the location of the pain and is usually elicited acutely if the tips of the fingers are pressed along the course of the ureter immediately above the brim. While it is quite true that actual pyelitis may be absent, yet pain may arise in the renal tract apart from infection, due to spasm of the ureter, tension of the dilated portion of the ureter above the pelvic brim, or to partial obstruction caused by kinks. A simple test is the passage of a catheter into the right ureter. Pain due to these causes is immediately relieved and also, in cases of severe pyrexia due to pyelitis, there is a rapid fall in the temperature and improvement in the pain. But while pain is often instantly and completely abolished by the direct relief of obstruction by passing the ureteric catheter, it may be sensibly relieved by any measure which will reduce the pressure of the uterus on the ureter. The patient will sometimes instinctively draw up the right leg to relieve the pain, as by so doing she softens the consistence of the psoas muscle and so reduces the counter-pressure on the ureter against the uterus. If she turns on her left side, especially while the uterus is yet not too large to fall away to the left, the pressure will be relieved, the ureter will empty, and the pain will disappear. But the surest and most satisfactory test is to pass a ureteric catheter whereby the dilated ureter can be entirely emptied. Relief of pain is almost immediate, a reaction which is very strong evidence of the reality of obstruction combined with atony as a cause of dilatation, stasis and pain.

### Treatment

The importance of pyelitis of pregnancy lies in the immediate, though not common possibility of extension of infection to the

renal tubules—pyelo-nephritis, and the remote risk of fibrotic changes in the ureter especially at the pelvi-ureteric junction and at the level of the brim of the pelvis causing obstruction hydro-ureter and hydronephrosis.

The risk of these later complications depends both upon the intensity of infection or upon the long duration of a milder infection.

It is therefore imperative to treat every case of pyelitis not only as an acute illness which must be relieved as soon as possible for its immediate disability, but also as a prophylactic measure against immediate extension to the kidney and later fibrosis and obstruction.

As the disease primarily depends upon stasis of urine in the ureter followed by infection, the general principles of treatment must be to relieve the stasis by establishing or encouraging drainage and disinfection of the urine by drugs.

Drainage can, where urgently necessary, always be secured at once by passing the ureteric catheter, except in a few cases where the catheter cannot be made to pass a pronounced S-shaped kink at the pelvic brim. It is not often, however, that ureteric catheterisation is necessary, but wherever the temperature is high and persistent, in spite of rest in bed and other treatment, the stagnant urine should be drained by the ureteric catheter. The ureter can be encouraged to drain itself by lying on the left side in bed and drawing up the right thigh, whereby the pressure of the uterus is partly removed and the firm consistence of the psoas muscle is softened.

Disinfection of the urine by specific drug treatment will be described in detail in the following sections.

There have been great advances in treatment since the days when the utmost that could be done was to give alkalinising doses of potassium citrate. Progress has been founded on observing the capacity for growth of *Bacillus coli* in urines of different pH. In a medium of acidity greater than pH 5.5 (i.e. below 5.5) the microbe is killed, and recent treatment has depended on a method by which the pH of the urine could be reduced to 5.3 or lower. The ketogenic diet was introduced in 1931 by Clark and Helmholtz (4). By reducing each element of the diet except fat to a minimum, a condition of ketosis is produced by which the pH of the urine can be reduced to five, or even less, in favourable cases. This method of acidifying the urine is successful in sterilising it in seven to ten days, but there are many failures

due to the impossibility of rendering the urine sufficiently acid, even by the most rigorously strict diet. Fuller (5) was able to show that the bactericidal principle in the urine is  $\beta$ -hydroxybutyric acid, but attempts to produce the same results by the administration of this acid failed because it is too rapidly oxidised in the blood. In 1935 Rosenheim (6) introduced mandelic acid ( $C_6H_5.CHOH.COOH$ ) which, by escaping oxidation, is excreted unchanged, and thus reduces the urinary pH when supplemented by ammonium chloride. This method of treatment has proved strikingly successful, though it is, unfortunately, peculiarly unpleasant for the patient. In 1936 Huber published a report on *B. coli* infections of the urine successfully treated by sulphanilamide, and still more recently Kenny, Johnston and Haebler (7) have shown the striking success which follows the use of this drug. It acts quickly in three or four days, and is less unpleasant for the patient.

During pregnancy, however, no method of treatment is likely to eradicate the infection permanently. Indeed, whenever there is a persisting cause of infection, as, for example, in calculous disease, tubercle or hydronephrosis, no amount of chemical sterilisation of the urine will effect a permanent cure. During pregnancy the atonic and obstructive dilatation of the ureter will provide a condition of stasis or ureteric retention of urine which will provide all the requirements necessary for a chronic or recurrent infection. It may be possible by mandelic acid or sulphanilamide to reduce very greatly, or temporarily abolish, the infection, yet should the ureter remain in a dilated atonic state it is almost certain that infection will appear in the urine again before delivery. Occasionally a cure may seem to persist right through pregnancy, but this is an exception. It can happen only in those patients, such as multiparæ, where the degree of dilatation is minimal.

After delivery the conditions are different. Now there is no obstruction, though atony may persist for a month or more. The action of mandelic acid or sulphanilamide may be complete and permanent, despite an atonic (though non-obstructive) dilatation, provided that a quick circulation of urine through the dilated portion can be obtained by active diuresis.

It is always desirable to increase the intake of fluid during the treatment of pyelitis, but where there may be a dilated ureter, as before and after delivery, this is specially important. Unfortunately it is, not compatible with treatment by mandelic



acid and its derivatives, since in the presence of free diuresis, a sufficiently low pH is beyond attainment.

During pregnancy little more can be expected than to hold the disease in check by occasional chemical disinfection of the urinary tract by one or other drugs just mentioned, combined, when possible, with a larger fluid intake and avoidance of all fatigue, chill, constipation and strong aperients.

The great majority of all cases are comparatively mild, but here and there we meet with a patient who is gravely ill with a high temperature and all the other features of severe bacterial toxæmia. It is probable that in these patients there is almost complete obstructive retention, combined with a virulent strain of infection. Here there is a real danger of pyelonephritis, and it is essential to treat by draining the ureter by means of a ureteric catheter. Relief of the retention is almost immediate in its effect, not only on the pyrexia, but on all the symptoms. In all such cases of acute illness it is almost certain that there must be some extension of infection into the renal tubules, but in the severe cases it reaches the degree of actual interference with the renal function. Traut (2) advises that the most reliable test of this is the figure of the total non-protein nitrogen of the blood, which should always be estimated in any case of doubt. He also suggests that if both kidneys are definitely infected, as shown by a real increase in T.N.P.N., the uterus should be emptied. Opinions must differ on this point.

Against this measure we must mention the risk of uterine infection in a case where there is an acute and virulent infection in close proximity. We recall a case in which the patient died after delivery from a generalised infection. A further difficulty is that induction of abortion tends to be very slow, or even a failure, by reason of the inertia of the uterus in cases of pyelitis. When we remember the probable endocrine origin of the cause of ureteric dilatation we can appreciate that this very condition could also be regarded as a cause for a similar uterine atony. Great delay in evacuation of the uterus, after some kind of intra-uterine interference, is an added cause of anxiety, for while the urinary stasis and infection is still unrelieved the uterus now is also liable to infection.

A greater difficulty is that when abortion is considered it is always at or after the fifth month, a time when the foetus is large enough to be impossible of removal at one operation (except by hysterotomy). Therefore it is questionable whether it

is good treatment to evacuate the uterus for even very severe pyelitis.

In the ureteric catheter, which may be left *in situ* for two or three days and repeatedly inserted if necessary, combined with mandelic acid or sulphanilamide, we have a method of treatment without danger and certain to relieve all acute risk to the kidney for the time being. After the seventh month there is a tendency to improvement in the tone of the ureter and the stasis of the urine, with consequent reduction in the severity of infection. It may be possible, therefore, to tide the patient over the dangerous middle period of pregnancy until there is a natural alleviation of the ureteric condition. The severe cases are always a great anxiety and must, sooner or later, raise the question of abortion. It seems a rational and radically curative measure, but it also has its dangers and anxieties, and, for the most part, we feel that here also it is wise to observe the general rule: treat the disease and leave the pregnancy alone.

**Mandelic Acid.** The use of this drug and the original ketogenic diet has been largely supplanted by sulphanilamide or sulphathiazole. However, we retain the original description of the use of mandelic acid as there are a number of varieties of coli infection which are not touched by the sulphonamide group. When mandelic acid was first introduced, it was given with ammonium chloride to ensure sufficient urinary acidity. Since the early days it has been chemically combined with ammonium chloride and sold under various trade names. In this form it is pleasanter to take than the original acid and salt.

The chief points in the technique of the treatment are to maintain complete regularity of dose so that none is omitted, and to restrict the daily intake of fluid to 2 pints or less. Unless the fluid is severely restricted it is impossible to reduce the pH of the urine to 5.5 or less. Above this figure the acidity is not sufficient to kill the organisms. The pH should be estimated each morning to check the efficacy of the treatment by adding a few drops of methyl red or universal indicator (B.D.H.) to half a test tube of urine. The colour table on the label of the bottle gives the figure of the pH.

Sometimes it is impossible to reduce the pH to 5.3 even by the strictest regard for the conditions of the treatment. In all such cases suspect the presence of *B. proteus* which by its capacity for splitting urea into ammonia can alkalis the urine and so neutralise part of the acidity produced by the mandelic acid. If it is difficult

to keep the pH down, reduce the diet as far as possible to a non-protein variety in order to diminish the excretion of urea, and increase fats relative to carbohydrates. The commonest error is to overlook the essential importance of restricting the fluids to not more than 2 pints of all intake (soups, tea, etc.) in twenty-four hours.

Complete failure to cure by mandelic acid properly administered or immediate reappearance of infection after the course has been completed, is probably due to a complicating organic condition such as calculus or tubercle.

Rosenheim's original recommendation in 1935 was to prescribe the following mixture :—

R Mandelic acid	.	.	.	3 grams
Sod. bicarb.	.	.	.	1-6 "
Aquam.	.	.	.	ad ʒi

R Ammon. chloride	.	.	.	1 gram
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in a cachet.

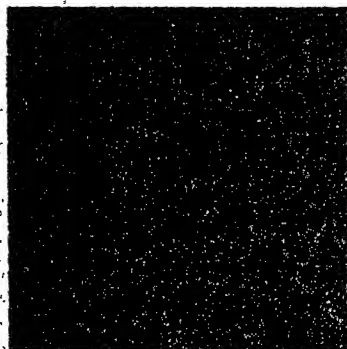
A dose of 1 oz. of the mixture is to be taken four times a day together with eight cachets of ammonium chloride daily. All fluids are to be restricted to not more than 2 pints.

The pH of the urine must be examined every morning by the indicator (methyl-red) to ensure that a sufficient degree of acidity is being maintained. The treatment must be maintained for ten to fourteen days, but in a favourable case the urine may be sterile in less than a week. Mandelic acid is mildly irritating to the kidney. Sometimes hyaline and granular casts and red blood cells are found in the urine, but they always disappear a few days after cessation of the treatment. The chief value of mandelic acid therapy is after labour when the ureteric conditions return to normal, and particularly for cases resistant to the sulphonamides. No longer is the obstructing pressure of the uterus acting on the ureter, and a short course of treatment can be relied upon to cure the patient finally.

**Sulphanilamide.** A great advance in the treatment of pyelitis due to coliform infections has been the use of sulphanilamide and allied drugs. It is usually possible to sterilise the urine within four days. Of the three drugs, sulphanilamide, sulphapyridine (M. and B. 693) and sulphathiazole (700) the best results and the least toxic effects follow the use of sulphanilamide and sulphathiazol. Sulphapyridine is more toxic in adequate doses of 1 gm. thrice daily. Sulphathiazol is nine times more potent against the organism *in vitro* than sulphapyridine, but it is absorbed and

excreted more rapidly and therefore not so easy to maintain in high blood concentration. Its excretion in crystalline form may lead to renal irritation and hæmaturia, but free fluids and sodium bicarbonate ( $\frac{1}{2}$  dram) given between meals reduces this tendency. In Fig. 5 we give a diagrammatic scheme of the result of treating a case of puerperal infection by *B. asiaticus*, showing complete sterilisation of the urine within three days. Not only does the urine become sterile, but symptoms disappear within forty-eight hours. Recurrence of bacilluria is liable to occur during pregnancy, but Kenny (7) claims that she has not had a puerperal case of recurrent illness or symptoms, and after delivery the cure seems complete. Persistent failure or immediate recurrence is due either to some important causal conditions being present and.

TAB. SULPHANILAMIDE 11 tds (total 45 grains  $\equiv$  3 grms. daily) given here



6,160,000 (29.1.38)



32,000 (30.4.38)



120 (31.1.38)



0 (1.2.38)

perhaps, unsuspected (*e.g.*, calculus, tubercle), or to a strain of infection which is not susceptible to the action of sulphanilamide. Not all strains of the coli group react equally well, some coliforms and streptococcus faecalis are completely resistant. Both cases of infection by these organisms often respond well to treatment by one of the mandelic acid derivatives. Sufficient work has not yet been done on the selectivity of the sulphanamide group in the treatment of urine infection.

### Relation of Pyelitis to Toxæmia

For years there has been speculation on the possibility of pyelitis as an antecedent to pregnancy toxæmia. On the surface it seems a reasonable assumption that pyelitis of sufficient severity or duration might, by extension into the tubules of the kidney, so damage them that their secretory efficiency becomes permanently

impaired. There have been many attempts to relate the sequence of toxæmia and pyelitis either in the same or a subsequent pregnancy. Peters and others have revived the discussion (14) and argued that there is a clear association between the two conditions. He finds that of 820 cases of toxæmia, 18% had previously suffered from pyelitis or pyelonephritis, and of 93 patients who had pyelitis 26% had hypertension or œdema or both before delivery. Other writers also have found a fairly close association between pyelonephritis and malignant hypertension.

It is probable that a severe condition of pyelonephritis will cause some irreparable damage to the kidneys, by which excretion generally is reduced and albumin allowed to pass. But the very large majority of all urinary infections in pregnancy—"pyelitis of pregnancy"—are mild and do not ascend the renal tubules as judged by impairment of secretion, retention of urea in the blood, or general severity of symptoms. Here and there we meet an exceptionally severe case of urinary infection in which these clinical features are obvious. It is such cases that might be expected to break down under the stress of pregnancy by showing an increase in tension, œdema, defective nitrogenous excretion, and albuminuria. But even here it is questionable whether the clinical condition is one of true pregnancy toxæmia ("pre-eclamptic toxæmia"). It is more likely to belong to the group now rather vaguely called "chronic nephritis" which invariably shows an exacerbation of symptoms during pregnancy.

Mussey and Lovelady (15) have reviewed the evidence and recorded their own experience. They point out that several other writers can find no association of the two conditions.

The general incidence of pyelitis in pregnant women is about 2% (Mayo Clinic) though some observers find bacilluria in a higher percentage. Mussey and Lovelady set out to answer the questions: (1) whether toxæmia developed during the course of pregnancies complicated by pyelitis or in subsequent pregnancies under their supervision, and (2) how many toxæmia patients had had a previous attack of pyelitis and how many had pyelitis during the puerperium. The usual clinical criteria were applied to define the diseases commonly known as pyelitis and toxæmia. The answer to their questions are: (1) of the 117 patients suffering or who had suffered from pyelitis (92 in pregnancy and 25 in the puerperium) 8 developed acute toxæmia (2.5%), which is a figure similar to the incidence of toxæmia in all pregnancies: (ii) of the 168 cases of acute hypertensive toxæmia, none had pyelitis before

the first pregnancy, but in 6 of the 163, pyelitis developed during the puerperium. Again the incidence of 2% corresponds to the liability of pyelitis in all pregnancies. These workers, therefore, conclude that "acute pyelitis of pregnancy is rarely either the indirect or direct cause of acute hypertensive toxæmia which arise in the course of pregnancy."

### Prognosis

The large majority of all cases of pyelitis of pregnancy and the puerperium recover completely, without risk of subsequent attacks, especially under modern methods of treatment. Severe and continued pyrexial illness is liable to be associated with extension of infection to the kidney, as we have already described. It is probable that there may also be later sequelæ. The function of the kidney can be impaired permanently, with the result that the reserve of the kidney is reduced.

During normal life this need not be very obvious, but a subsequent pregnancy may cause a strain on a "low reserve" kidney and that form of albuminuria usually described as "chronic nephritis."

We have already stated that in most normal women the dilatation and atony of the ureter during pregnancy disappears within a month or so after delivery. In some the non-pregnant conditions are reached within ten days, but in others the involution may not be complete in two months, and it is possible that, even after completely normal pregnancy, the ureters and renal pelvis may occasionally be subject to some degree of permanent dilatation:

The subsequent state of the ureters is, however, very different where the patient has suffered from pyelitis during pregnancy and the puerperium. McConnell and Gray (16) after pyelographic examination of 28 patients who had had moderate or severe pyelitis during pregnancy (22 cases) or the puerperium (6 cases), reported that morbid conditions of the renal pelvis and ureter could be found as long as fourteen years after the febrile attack. They found normal pyelograms in only 2 women, 1 after five months and 1 after five years. The remainder had some degree of dilatation in 17 of whom it is described as moderate or severe. In 2 cases there were calculi, and in one, very deficient secretion.

Clinically these patients showed varying symptoms. Nine women complained of no trouble, but the rest had backache and pains in the left or right side. It is possible that some of the

patients whom we see long after delivery complaining of vague pains in the side and back, even though the urine may be normal, are suffering from some degree of tract dilatation which first appeared during pyelitis of a previous pregnancy. In hospital and other clinics, patients complaining of pain in the back and left side are usually dismissed as suffering from "cervicitis," constipation, an orthopaedic lesion, or even prolapse, but in the light of much recent investigation of the condition of the kidneys and ureters after pyelitis, it would be well to investigate these patients by intravenous pyelogram.

Jacobi (13) also describes permanent changes in that part of the ureter above the point of compression at the pelvic brim. The normal atony and dilatation disappears in nearly every woman after the puerperium, but if a prolonged and severe infection has been present the dilatation may be permanent by reason of destruction of the muscle or neuro-muscular mechanism of the ureteric wall and deposition of scar tissue. He calls this condition a "fixed pregnancy atony of the ureter." It is important because normal peristalsis is impeded, and ureteric retention of urine and chronic infection are the results.

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## CHAPTER V

### ANÆSTHESIA AND ANALGESIA IN OBSTETRICS

DURING the past few years there has been a great increase in the amount of attention paid to this subject. Doctors are interested to find out the best methods of producing analgesia or—at least—amnesia, and members of the laity are insistent to know what steps are going to be taken to ease their pains. Every parturient woman now expects something to be done for her relief.

In the past it has been customary to administer some mild sedative as soon as labour has become definitely established, the cervix is beginning to dilate and the woman is commencing to feel some distress. For this purpose potassium bromide gr. 15 and chloral hydrate gr. 20 are widely used, and very rightly so even by midwives. It is still one of the safest and best things in their hands. It also has the advantage that the dose can be repeated as desired and it may possibly aid the relaxation of the cervix. Until recently the majority of doctors have also been content with this or some similar combination of sedatives, perhaps including in the mixture Tinct. opii, ℥vii, but other and stronger drugs are now in general use. The more conservative among us may still prefer to give chloral and bromide in the very early stages and thus to delay the use of the more powerful weapons until some hours later when a greater analgesic effect may be required. Those who are of this mind must particularly remember the danger of giving morphia too near the time of delivery of the foetus.

When we consider the various drugs other than chloral and bromide which are at our disposal it will quickly be appreciated that the only true analgesics are opium and its derivatives. Most of the others act largely as hypnotics. It is for this reason that the combination of morphia with something else is so widely used. For thereby analgesia, reinforced by amnesia, is produced.

But morphia has a depressant action on the child's respiratory centre and must never be given within, say, three hours of delivery. Also it is generally considered to delay labour, but this is open to doubt. It has been shown by Bourne and Burn (1) that morphia increases the intervals between the uterine contractions but at the same time it lengthens the time over which each contraction



lasts. Theoretically therefore its use might diminish the duration of the first stage. It certainly gives relief from the pains and longer rests between them. Fig. 7 is a graph of intra-uterine pressure changes, or in other words, labour pains, before and after giving morphia. The tracing was obtained by insertion into a parturient uterus of a small water-filled bag connected with a manometer. The rise and fall of the mercury column was communicated to a writing point which traced its movements on a slowly moving drum.

It is quite a common practice nowadays to give morphia together with scopolamine, with or without the previous exhibition of chloral and bromide. The first injection is given when labour is really well started—say when the cervix is sufficiently dilated to admit the tips of two fingers. To produce reasonably adequate obstetric analgesia it is usually found that a fairly heavy dose of morphia and scopolamine is required. But it is unwise to start with a

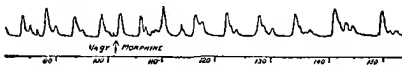


FIG. 7.

big dose. Small doses can easily be repeated. Large doses, which in a susceptible patient are producing alarming effects, cannot be extracted. Therefore start with morphia gr.  $\frac{1}{2}$ , scopolamine gr.  $\frac{1}{100}$ , or even  $\frac{1}{200}$ . The effect of this will not become evident at first. But do not be tempted to give the second dose (in the same quantities) until at least one hour after the first injection. As an alternative to morphia, "omnupon" is preferred by many in the dosage of gr.  $\frac{1}{2}$ . If it is desired to produce a deep effect, it is necessary to use big doses as, say, omnupon gr.  $\frac{1}{2}$ , hyoscine gr.  $\frac{1}{50}$ . Again it may be emphasised that if such big doses are to be given it is a wise precaution to give only half the above quantities at the first injection in case there be any idiosyncrasy to either of the drugs. If after the lapse of one hour no abnormal effect has been produced, the remaining half can be given.

In many cases this will give such relief to the patient in the first stage of labour that nothing else is required until the onset of expulsive pains. But in others, and particularly in cases of elderly primigravidae or in women with a protracted first stage,

something more is required to give a sufficiently prolonged effect. To this end some employ, as an alternative to a big dose of morphia and scopolamine, morphia in smaller doses, gr.  $\frac{1}{4}$  to gr.  $\frac{1}{16}$ , but given intramuscularly in solution in 2 c.c. of a 50% solution of magnesium sulphate. It is claimed that the action of the morphia is thereby intensified and prolonged—also that by giving a further 2 c.c. of the magnesium sulphate solution (without the morphia) a further prolongation of the effect is produced. This does not appear to work to the satisfaction of everybody, and therefore if, as should be the case, it be our object to reduce for all women in labour physical suffering, mental distress and fear of a subsequent labour to a minimum, the cases of slow dilatation of the cervix offer a great field for the exercise of skill in bringing this relief. Here, for example, the technique of "twilight sleep" may be followed. It would be better perhaps to say a modified technique since it is usual nowadays to discontinue the scopolamine injections some little time before the actual birth of the child—by prolonging them to the actual time of delivery, the life of the child is generally considered to be endangered.

### Morphia-Scopolamine Analgesia

It is remarkable that such things should happen but as recently as 1939 Schulze (2) argued that twilight sleep should be dispensed with in most cases as it withholds from mothers the joy of having suffered for their children! Such views can be ignored.

In the employment of a modified twilight sleep technique it is necessary to give the first injection of morphia gr.  $\frac{1}{4}$  and scopolamine gr.  $\frac{1}{160}$  before the mother is tired and before uterine action has become at all irregular. It must be remembered that its effect hardly becomes manifest until the expiry of fully a quarter or even half an hour and that the effect of the injection has largely disappeared after three, or at any rate four hours. Griffith and Goodall (3) consider that twilight sleep has been unjustly abused and deem it the "most effective first stage treatment." They postulate two rules: (a) that the first dose must be small and that the repeat doses must be graded to suit the requirements of each individual patient. Their suggested initial dose is morphine gr.  $\frac{1}{4}$ , hyoscine hydrobromide gr.  $\frac{1}{150}$ , Atropin sulphate gr.  $\frac{1}{150}$ . One to two hours later they give their first repeat dose in which the atropin may be omitted if a deep effect is required. They do, however, advise at least one dose of atropin despite its unpleasant effect in causing dryness of the

throat, for in their view it lessens the depressive effect on the foetal respiratory centre; (b) the full force of the drug action must not be allowed to impinge on the second stage of labour.

Should further analgesia be required after the effect of the first one or two doses of morphine and hyoscine has largely passed off, continuing doses of scopolamine gr.  $\frac{1}{16}$  are administered subcutaneously at about hourly intervals. After the second or third dose it is advisable to control the dosage by the employment of the "memory test." The patient when awakened for a drink, or for an injection is shown some familiar object. If she is unable to recognise it, or is unable when next awakened to remember what she has been shown, the amnesia is of satisfactory degree. This is also shown by the patient being asleep between the pains and yet waking up and even appearing to be fairly alert during the contractions. But this appearance of alertness is deceptive. Subsequently she will be found to have little or no memory of her sufferings.

It is unfortunate that all women do not respond to the treatment in the same manner. Tremendous individual variations are observed. Some women will react perfectly, some will become very restless and an occasional one, almost maniacal. In such patients the hyoscine must be stopped at once. In others, overdosage is indicated by an increased pulse rate and a slowing of respiration.

In all cases certain precautions must be observed. Thirst is a common complaint and water must be given whenever the woman is sufficiently awake to drink. She must never be left alone, particularly must she never be unattended when poisonous lotions are near at hand. For her thirst may lead her, in her confused mental state, to drink these with disastrous effects. The bladder must be watched carefully, since the patient under "twilight sleep" is unaware of any desire to micturate and considerable distention will occur unless relieved, if necessary, by a catheter.

The scopolamine injections may be continued over many hours in a patient who is responding well. The intervals between the doses may, however, be progressively lengthened as time goes on. But when the second stage has clearly started it is customary to discontinue the injections and to employ one or other of the inhalation anæsthetics which are more properly applicable to that stage of labour and which will later be discussed.

Apart from the danger of overdosage and the risk of some women becoming excitable and violent as the result of the scopolamine

injections, all cases of "twilight sleep" have the disadvantage that there is a lessening of the expulsive forces, thus leading to an increased forceps rate and a consequent greater danger of lacerations and perhaps of puerperal pyrexia. A further disadvantage that must be borne in mind is that the child is frequently suffering from depression of its respiratory centre. But in the vast majority of cases it will recover if kept still and warmed, and if it is given an injection of lobeline into the umbilical vein the blood containing the injected alkaloid being massaged into the foetal circulation by "milking" the cord towards the child's abdomen. Prior to this, of course, the air passages must have been cleared and oxygen must be blowing gently into the nasopharynx through a nasal catheter.

Despite its occasionally manifest disadvantages it will be generally agreed that morphia-scopolamine analgesia is of particular value in cases of prolonged first stage consequent upon primary uterine inertia and in cases with a "rigid cervix." A series of smaller doses, or of similar doses at longer intervals, will be found of great help in normal cases in sensitive or nervous women and should be much more generally employed than is now customary.

In spite of some criticism directed against "twilight sleep" and despite the fact that some of the criticisms appear to have been directed chiefly against scopolamine, a few obstetricians have found this drug alone of great value in midwifery. It has been used in doses far larger than those already described. For example, Green-Armytage (4) has stated that it has no effect on the child, shortens labour and is in no way dangerous if there is no toxæmia. He advises  $\frac{1}{100}$  gr. every half hour for three doses when labour has properly started. He then gives  $\frac{1}{200}$  gr. every two hours; and of these usually three injections are required. In addition, a few whiffs of chloroform may be given if necessary when "crowning" has taken place. His contention that hyoscine does not adversely affect the child is supported by Stevens (5) and receives indirect support from Clifford and Irving (6) in the article, which is more extensively referred to below. But it appears to be a general clinical opinion (for which one can find but little published evidence) that scopolamine is dangerous to the child. Further evidence on this point will be of interest.

### The Barbiturates

Much has been written of the value of the various barbiturates—nembutal, sodium amytal, evipan, etc.—in obstetrics, but since

the last edition of this book we have found that their use is becoming less and less general. This is probably because of their very variable effects in different patients. One woman may react perfectly. She will be quiet and practically asleep during labour and have no subsequent memory of any suffering. The next one, treated in exactly the same manner, may become uncontrollably excited. Furthermore, they can no longer be regarded as harmless to the baby—the child is often born under the influence of the drug and resuscitation may be difficult. In fact if a list were compiled placing the drugs used for obstetric analgesia in order of their danger to the baby, morphia would probably be regarded as the most dangerous and paraldehyde as the least. And it is likely that many obstetricians would put the barbiturates near the morphia end of the scale.

As already stated, these drugs act as soporifics, not as true analgesics, so that they act by abolishing memory rather than by relieving pain. Griffith and Goodall (3) further point out, that in view of this characteristic of their action these drugs may, in sufficient dosage, abolish a patient's knowledge of the pains of labour but fail to protect her nervous system against the trauma of repeated painful afferent stimuli.

Nevertheless, these barbiturates still find many advocates and a brief survey of the methods in which they can be employed, may be permitted. Their action is best employed only during the first stage of labour. When the second stage commences a change to one of the inhalation anæsthetics is called for.

**Sodium Evipan.** One of the great disadvantages of the barbiturates, to which reference has already been made, is that their effect is variable. This could to a large extent be eliminated by accurate dosage judged by the depth of narcosis produced. This accuracy can only be achieved by the intravenous administration of the drug by a skilled anæsthetist conversant with its effects. And the barbiturate which best lends itself to this method of administration is sodium evipan. A 10% solution (1 gm. dissolved in 10 c.c. of distilled water) is used and small doses of 2 c.c. are given at intervals. Samuel (7) advises rather larger doses. His initial dose is 4 to 5 c.c. given at about the time when the cervix is dilated to the size of a two-shilling piece. The repeat doses are from 2 to 3 c.c. given on the commencement of return to consciousness. He has given as much as 18 c.c. in all during a labour lasting thirty-six hours. He also claims that sodium evipan does not affect the babies even when used

as a basal anaesthetic before Cæsarean section. We feel that most people would not agree with this statement, and it is flatly contradicted by Holterman (8).

Pernocton is also given by the intravenous route and must be given very slowly—at least one minute, better a minute and a half, should be spent over the injection of each cubic centimetre. It is put up in ampoules of 2.2 c.c., and the dosage is about 1 c.c. for each 30 lb. weight of the patient; *e.g.*, a patient of 150 lb. requires about 2½ ampoules as the maximum dose. The injection should be given when the first stage of labour is well established, and the duration of sleep is from two to four hours. If the patient awakens from the hypnosis and delivery is not to be expected for three or four hours, an additional 2.2 c.c. may be given. But on this occasion two minutes must be spent over the injection of each cubic centimetre and the second injection must not be given less than three hours after the first. Kantz (9) has reported a number of cases treated on these lines, and Brammer (10) has recommended the combination of this drug with pituitary extract to eliminate the weakening of the pains which temporarily follow the giving of pernocton. He recommends as the initial dose 3 to 4 c.c. of pernocton intravenously, 1 to 2 c.c. intramuscularly and 0.5 c.c. of pituitary extract intramuscularly. Additional injections of 1 to 2 c.c. of pernocton intravenously and intramuscularly with 0.5 c.c. of pituitary extract are usually required after the lapse of three hours or more.

A new use has recently been suggested for pernocton, *viz.*, to replace the preliminary morphine injection in twilight sleep. Claye (11) advises a minimal intravenous dose to produce a quick amnesia which can be prolonged for many hours by judicious scopolamine medication. It would seem to be a scheme deserving of extended trial.

Other drugs of the barbiturate series which have been tried intravenously are nembutal and sodium amytal, but they do not seem to have been great successes or to be particularly safe. In common with the other barbiturates they suffer from four great disadvantages: (1) there is no specific counteractive drug in cases of overdosage, (2) the patient tosses about during each contraction and needs constant attention, (3) sloughs will form if any of the drug is given outside the vein selected; and the restlessness of the patient during a pain may make this very difficult to avoid, and (4) the intravenous method of administration is quite unsuitable for domestic midwifery however interesting

and exciting it may be for expert anæsthetists on whole time and salaried appointments in obstetric hospitals.

If we now consider the question of oral administration, we find that the barbiturates most commonly employed in this way are nembutal, sodium amytal and seconal.

Nembutal is supplied in capsules of  $1\frac{1}{2}$  gr. each and the initial dose is two capsules. Subsequently one capsule is given at about two- or three-hourly intervals. O'Sullivan and Craner (12) advocate the combination of nembutal and chloral. When the cervix (in a primigravida) is  $\frac{2}{3}$  to  $\frac{3}{4}$  dilated they give 8 gr. of nembutal. Ten minutes later, chloral hydrate gr. 30 in 8 oz. of a well-sweetened home-made lemonade is administered. Subsequent doses are nembutal gr.  $1\frac{1}{2}$  and chloral hydrate gr. 30. The first "repeat" dose is given two hours after the initial one, and subsequent "repeat" doses every three hours. In each case the nembutal must precede the chloral by ten minutes. As in the case of all the first-stage analgesics already mentioned, some form of inhalation anæsthesia is required for the actual delivery. A closely similar method was used with success by Mallinson (13) who claimed to have had only 3% of failures though restlessness of the patient is admitted as one of the disadvantages of the method. His patients were found to need only whiffs of ether during the expulsive stage in the majority of cases. He stresses the points that morphia, hyoscine and chloroform are all dangerous adjuvants which must be avoided and thinks that if nembutal and chloral only are used to produce analgesia during a labour, the baby will give no cause for alarm. Furthermore the use of chloral helps the analgesia and tends to reduce the incidence of excitement for which nembutal alone is often held responsible. Rosenfield and Davidoff (14) advise larger doses of nembutal than most people, and combine with it rectal paraldehyde. They give  $4\frac{1}{2}$  gr. as soon as labour is established and the preparatory enema given. Fifteen minutes later another 3 gr., and this is followed by the rectal administration of 6 drachms of paraldehyde in  $1\frac{1}{2}$  oz. of olive oil. A pad over the anus and the inhalation of nitrous oxide is used to prevent the expulsion of the paraldehyde. Sometimes  $1\frac{1}{2}$  to 3 gr. of nembutal is again given if the paraldehyde effect passes off. During the expulsion of the child they recommend gas and oxygen. They admit marked restlessness in 7.83% of their cases, but claim that the average primiparous labour lasted only nine and three-quarter hours, while the average duration of analgesia and amnesia was eight hours.

The majority of writers would not approve of quite such large doses as these two advise, though Clifford and Irving (6) say that the average dose of pentobarbital (a synonym of nembutal) in their recent series of cases was 7.5 gr., while some received 9 gr. or more.

We have here an example of divergence of opinion among obstetric experts. It has already been indicated that the general drift of opinion seems to be away from the barbiturates and back to morphia-hyoscine as the method of analgesia to be selected for the first stage of labour. But nobody can afford to ignore Irving's opinion and he and his colleagues have been steadfast advocates of the barbituric acid compounds. They state (*loc. cit.*) that it would appear from their figures that the general use of sodium amytal and pentobarbital in their (Boston) clinic "has had no ill effect on the life of either the foetus or the new-born infant." Further they "issue a warning against the use of any analgesic containing an opium derivative" though they sometimes use scopolamine or rectal ether as adjuvants to pentobarbital. The addition of scopolamine is said to give better results as regards obstetrical analgesia without exerting an unfavourable influence upon the infant at birth. So far this seems to be only an occasional addition to their barbiturate therapy and not yet to have become established as a routine.

**Sodium Amytal.** Capsules contain 3 gr. each. The excretion of this drug is less rapid than that of nembutal, and the hypnosis produced should theoretically be of longer duration if of lesser intensity. The usual initial dose is 3 to 6 gr. with subsequently 3 gr. as required, *i.e.*, usually at two-hourly intervals at first with longer intervals later. Culum and Bartholomew (15) recommend the combination of this drug with paraldehyde and give 3 gr. at about 3 cm. dilatation of the cervix. Half an hour to one hour later a second 3 gr. is given if all is going well, and within half an hour of this 6 to 8 drachms of paraldehyde in an equal bulk of olive oil is injected into the rectum.

Generally speaking, one hears little of sodium amytal nowadays and one observes that Irving and Clifford have abandoned it in favour of pentobarbital (nembutal).

Seconal is also supplied in 1½ gr. capsules and has been advocated for first stage analgesia. The initial dose is two capsules (3 gr.) and "repeat" doses of 1½ gr. can be given at one- to three-hour intervals, according to the individual patient's response. In no case of ordinary duration should a total dosage of 12 gr. be



exceeded. With the onset of the second stage it is preferable, with this as with the other barbiturates, to change to one of the gaseous anæsthetics.

### Paraldehyde

Mention of this drug has already been made in the above section. Its administration by the rectal route seems to be becoming increasingly popular, although it again is somewhat variable in its effects. It is given in doses of 6 to 8 drachms (according to the weight of the woman) in 6 to 10 oz. of normal saline solution or in 4 oz. of olive oil. This latter seems to be preferable as it diminishes the incidence of proctitis.

If barbiturates are not being used, it is desirable to precede the paraldehyde by a hypodermic injection such as morphia gr.  $\frac{1}{2}$ , scopolamine gr.  $\frac{1}{100}$ , or 1 c.c. of opoidine in 2 c.c. of 50% magnesium sulphate solution. Such injections allow the administration of the paraldehyde to be delayed until its maximum effect is required, and they also assist the analgesic effect.

One of the difficulties to be overcome is that of getting the paraldehyde mixture sufficiently high into the rectum. Another is to prevent its expulsion. If the head is low in the pelvis great difficulty may be experienced in getting the rectal tube above the presenting part. But it is necessary that this be done if a successful result is to be hoped for. The injection should be given slowly and on its completion a pad should be kept pressed against the anus continuously for a short time and then at intervals if there is any sign of expulsion of the drug during a pain. In a satisfactory case there may be deep sleep for up to six hours and if one of the inhalation anæsthetics is used during the stage of delivery the patient may have little or no knowledge of the confinement through which she has just passed.

### Rectal Ether

The development of this method of producing obstetric analgesia is primarily associated with the name of Gwathmey. For many years he made use of the combination of morphia and magnesium sulphate as a preparation for the ether. He gave  $\frac{1}{2}$  or  $\frac{3}{4}$  gr. of morphia in 2 c.c. of 50% solution of magnesium sulphate at about 3 cm. dilatation of the cervix. He procured an extension of the analgesic action of the morphia by giving a further 2 c.c. of the magnesium sulphate solution later on if required. More

ntly he appears to have substituted nembatal for the morphia. athmey and McCormick (16) have recently described their lern technique in which nembatal is used as the basal esthetic and in which the mixture for rectal administration been slightly changed. It is now

Ether,  $2\frac{1}{2}$  oz.

Alkaloidal quinine, 20 gr.

Alcohol, 45 minims.

Paraldehyde, 2 drachms.

Olive oil, to 4 oz.

ie quinine is first dissolved in the alcohol, and the paraldehyde, her and oil are subsequently added in this order; the mixture then stirred and strained.

At the B.M.A. meeting in Oxford in July, 1936, Dr. Lloyd-Williams described her experience with a slightly different chnique. Early in labour she gave 30 gr. each of potassium omide and chloral hydrate. When the patient became distressed c.c. of opoidine in 2 c.c. of 50% magnesium sulphate solution as injected intramuscularly. If no relief followed in twenty r thirty minutes rectal ether was given by gravity according to hawthmey's old formula, viz.:

Quinine, 20 gr.

Alcohol, 40 minims.

Ether,  $2\frac{1}{2}$  oz.

Olive oil, to 4 oz.

She stated that the injection could be repeated after an interval of not less than four hours.

It is claimed by Gwathmey that satisfactory analgesic effects are secured in 85% to 95% of cases, that the patient is more co-operative than in "twilight sleep" analgesia, that the instillation remains effective for two to six hours, that no ill-effects are produced on the child, and that forceps deliveries are decreased in number. Other workers have not been so successful as this. Perhaps it is only lack of experience in the method which has led an occasional writer to report poor success in small series of cases. But the fact remains that other workers have not been able to reach the high level of success claimed by Gwathmey.

One word of warning is required. Gas and air or gas and oxygen may be used during the actual birth of the child, but chloroform must never be used in conjunction with rectal ether.

**ANÆSTHETICS IN THE SECOND STAGE OF LABOUR**

The foregoing part of this chapter has been devoted to drugs which are of value in giving relief to pain during the first stage of labour and which continue to give some benefit during the second stage. But there are two periods in labour which seem to be specially painful, one being the descent of the head into the vagina early in the second stage and the other being the actual delivery. For these two times, and, to a somewhat lesser extent, during the intervening part of the second stage, some form of inhalation anæsthesia is required if we are to provide the maximum possible relief.

The phrase "inhalation anæsthesia" has been deliberately chosen, for such methods as extra-dural nerve blocking, rectal avertin, etc., can be dismissed as useless or dangerous. Griffith and Goodall (3) say that "spinal, caudal, local and perineal (anæsthetics) have been chiefly experimental and rightly short-lived." We agree. So we will turn to the discussion of the inhalation anæsthetics during which we will first consider the one which we regard as the best, viz., gas and oxygen.

**Gas and Oxygen**

Gas and oxygen has obvious disadvantages. It needs a special apparatus (though this can be hired), it needs a skilled administrator who will have, on many occasions, to give up several hours of his time to an obstetric case, it is expensive in service and in material, and lastly—a point often forgotten by its advocates—the woman in labour has to be allowed to recover consciousness between each pain; each time she wonders—and frequently asks—"Is it all over yet." Nevertheless if a woman has been carried fairly comfortably through the first stage of labour by morphia-scopolamine or other analgesia, and if her second stage is conducted with the aid of intermittent gas and oxygen anæsthesia she is, in our view, being spared suffering to the best of our present skill and knowledge. For gas and oxygen has no slowing effect on the expulsive forces and has no unpleasant after-effects on the mother. Clinically, too, it seldom appears adversely to affect the child, though such an effect is theoretically possible as shown by Eastman's researches (*vide infra*).

Various forms of gas and oxygen apparatus have been devised whereby the mother can give herself inhalations as desired. But these are not satisfactory, and to secure the best results the

anæsthetic should be administered by one skilled in its use—particularly as he may require to add a little ether for any operative procedure or during the actual delivery of the head. The effect of nitrous oxide given during the first stage of labour with feeble

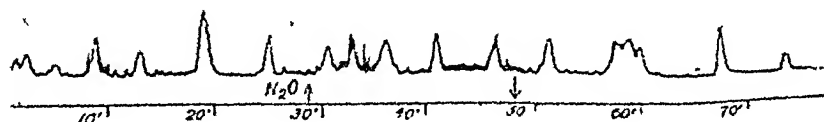


FIG. 8.

and irregular pains is shown in Fig. 8. There is no material change in the character of the contractions.

### Chloroform

Should gas-oxygen anæsthesia be unobtainable, then for normal obstetric cases chloroform is *generally* the most useful substitute. It appears to be the popular anæsthetic for *private* obstetrics in Canada, though in the United States ether is preferred. The best way to use chloroform is in a Junker's inhaler and if the mask is put into the patient's left hand and the pressure bulb into her right, it will be found that by means of a few good squeezes of the bulb and a few deep inhalations at the commencement of each pain she is able greatly to relieve her sufferings and yet still be able to employ her accessory expulsive forces. When the head is distending the perineum the nurse should take charge of the bulb. As soon as the obstetrician detects the first sign of a

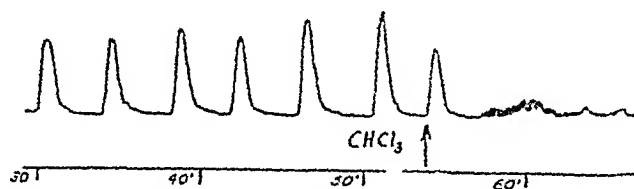


FIG. 9.

contraction he signals to the nurse who pumps chloroform vapour under his direction. In this way a more or less complete degree of anæsthesia can be secured with safety during the expulsion of the child, and, if necessary, during the time subsequently required for the repair of any lacerations. And at the end of it all one is surprised to find that only 3, or 4 drachms of chloroform have been

used. This is of great importance, for it must be realised that full chloroform anæsthesia must not be used during any prolonged obstetric manipulation. Under these circumstances, for fear of delayed chloroform poisoning, the services of an anæsthetist must be secured and his anæsthetic will usually be ether. Ethylene is generally inadvisable in domiciliary obstetrics as there is so frequently a fire in the room and consequently there would be grave danger of an explosion. The same objection applies to the use of ether.

A disadvantage of chloroform (and the same applies to ether) is that it has a depressant action on the uterine contractions during the first and second stages (Bourne and Burn). Fig. 9 shows the effect of chloroform inhalation during the first stage of a normal labour. Fig. 10 illustrates the action on the uterus during



FIG. 10.

the second stage of labour when the uterine contractions are much stronger, and more frequent. The depressant effect appears immediately on the exhibition of the anæsthetic and is therefore probably due not to a direct action on the uterus but to sympathetic stimulation which is inhibitory to labour.

Nevertheless, in practice, if chloroform is given as above described, only at the commencement of each contraction and not during the intervals, it appears clinically to have little or no slowing effect on the progress of labour in the great majority of cases. When chloroform was used as a routine for every delivery at Queen Charlotte's Hospital there was found to be no increase in the time of labour, an unchanged forceps rate, no greater incidence of post-partum hæmorrhage and no greater still-birth rate.

Many forms of inhaler for the administration of chloroform in

obstetrics have been described, and each has its advocates, but they hardly call for detailed description in this book. The general idea in the case of these inhalers is to provide only such a concentration of chloroform as is safe and so to place at the disposal of everybody a method of giving relief from the pains of the second stage of labour which may be safely and universally employed. The same idea was the basis for the employment of small glass capsules of chloroform (similar to amyl nitrate capsules) which received trial for a considerable time but which have been entirely superseded by the methods by which gas and air is self-administered. Objection to the use of chloroform in labour is reinforced by the views of Gilliatt and others who fear its toxic effect on the liver. Buschbeck states that it has not been used in the Würzburg clinic since 1923, and there (as in many German clinics) acetylene and oxygen has been extensively tried. This, however, meets no favourable reception in this country on

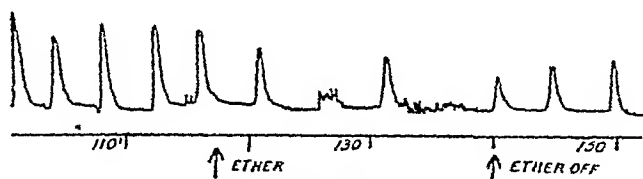


FIG. 11.

account of the risk of explosion. The same applies to ether which he recommends. Gilliatt also prefers ether to chloroform though he thinks gas and oxygen greatly preferable to ether. It is sometimes thought that ether stimulates the uterus. Its effect is, however, almost as inhibitory as chloroform, as can be seen from the graph (Fig. 11). In this case the bag was inserted into the uterus during the first stage of normal labour. The inhalation of ether produced an almost immediate reduction in uterine work. The prompt recovery of the uterus after stopping the ether is remarkable. It may be noted in passing that cyclopropane does not inhibit uterine contractions. On the contrary it probably stimulates them. Though this anæsthetic may be of value in cases of Cæsarean section (*vide infra*) it is not a suitable one for normal obstetrics.

To return to the consideration of chloroform, the fact remains that despite the objections it will doubtless continue to be used because of its relative cheapness and its portability. But because of its advantages it is a fortunate thing that there has been

developed recently a safe and relatively efficient method of inhalation anæsthesia for the second stage of labour, that is, the administration of gas and air.

### Gas and Air

We owe the development of this method of treatment largely to Minnitt (10) among whose many publications on the subject, the short article quoted is one of the most recent. Various forms of apparatus have been designed for the administration of this mixture of gas and air, and happily some of them, such as one of the Minnitt types and the Queen Charlotte's type, are fairly portable. The principles of the action of the apparatus of whatever type is that the mixture inspired is constant and that only active inspiration by the patient makes the supply of the mixture available. The concentration of nitrous oxide in air varies somewhat in the different types, but about 45% to 60% is an average figure. About 35 gallons of nitrous oxide are consumed per hour.

There seems to be a popular idea that nitrous oxide is quite harmless to the baby and therefore its use is without risk in cases of labour and for Cæsarean section.

This is not quite true, as has been shown by Eastman (20) at the Johns Hopkins Hospital. His conclusions may be quoted: "Nitrous oxide mixtures administered to mothers in proportions of 85 : 15 or weaker and for periods of less than five minutes, regularly cause moderate degrees of foetal anoxæmia but the normal full time infant is apparently not harmed. When nitrous oxide-oxygen is given in concentrations of 90 : 10 or stronger over periods which exceed five minutes, marked degrees of foetal anoxæmia are produced in about one baby out of three and occasionally profound asphyxia neonatorum results."

When it is remembered that Eastman is speaking of gas-oxygen mixtures it will be realised that the gas-air mixtures, even if only 50 : 50 are not entirely devoid of effect on the foetus. But the limited periods of administration should make the foetal risk negligible. The subject will again be mentioned when the anæsthetics for Cæsarean section are considered. For the moment we will return to the matter of self-induced anæsthesia by gas-air mixtures.

With regard to the technique of administration: the patient should be made aware of the method of using the apparatus very early in labour, long before she needs to use it seriously. She

must be instructed as to how to close with her finger the air-hole in the mask of the Minnitt apparatus, for if this hole is not occluded, only air will be inhaled. Care must also be taken to see that the mask fits the face accurately. Gas and air anaesthesia may be started during the first stage of labour, but it is preferable that some form of premedication, such as a modified twilight sleep, should form the preliminary. During the second stage of labour it is particularly important that the inhalations should be started on the very first sign of a pain. Seven or eight quick breaths should be taken and then the patient, though relieved of much of her suffering, may remain sufficiently co-operative to hold her breath and to force down if so directed. At the time of actual delivery, the patient should be inhaling from the face-piece as quickly as possible. But it will often be found that for the perineal stage something more than gas and air—perhaps gas and oxygen or chloroform—is required. A few contra-indications to the use of gas and air analgesia in labour should be mentioned, but it will at once be realised that these indicate grave medical complications and form no argument against the use of this method for normal cases. The objections are cases of heart disease of all but the slight degrees, patients with albuminuria and raised blood pressure in danger of eclampsia, and patients with pulmonary tuberculosis, bronchitis or other active lung diseases.

A modified use for nitrous oxide in labour has recently been suggested at the Royal Society of Medicine by Chassar Moir. He showed an apparatus by which a limited quantity only of pure nitrous oxide was delivered to the patient on her active inspiration into the face-piece at the commencement of each pain. The idea is that enough gas can be provided at the very start of each contraction to give relief from pain and amnesia and yet be not enough to produce cyanosis. The principle of the action is thus quite different from that of the more established types of gas and air apparatus, and it will be of interest to see what results are obtained when sufficient cases have thus been treated.

A variation of Chassar Moir's principle has been described by Elam (21), whose apparatus is so constructed as to give an initial limited dose of pure nitrous oxide when the patient first commences each series of inspirations from it. Thereafter, instead of the patient having to make the effects of this dose of gas suffice, the apparatus supplies a mixture of 50% nitrous oxide in air which will keep the analgesia going as long as is requisite.

If Chassar Moir's or Elam's apparatus is found to give satis-



factory analgesia and at the same time to be free from danger to the child it will go far to remove the great disadvantage from gas and air analgesia by the self-administration methods at present in wider use, namely the disadvantage that the action of the anæsthetic is not quite enough. The patient may breathe gas and air as rapidly as she can, but the pain has often become of great intensity before the analgesic effects of the gas and air have become manifest. Alternatively the degree of anæsthesia secured may never reach a sufficient depth

### Spinal Anæsthesia

Spinal anæsthesia has been extensively used for the second stage of labour, but finds no favour in this country despite the fact that the child is unaffected and that there is no danger of post-partum hæmorrhage. No further reference to this method is needed at this point, but further consideration will have to be given to it in the next section.

### Sacral Anæsthesia

Sacral anæsthesia in obstetrics has again reared its ugly head. Poole (22) quotes the earlier work of Oldham and of Knauer and reports 32 cases of his own in which he used 25 to 45 c.c. of a 0.1% solution of percaine in normal saline, not water. Ten of the 32 cases were deemed failures but all such failures were judged to be "preventable." Poole describes the principles of sacral anæsthesia and the technique to be employed. The duration of good anæsthesia is stated to average four hours but quite commonly, especially if the injection has been given before the pains are regular and very strong, the frequency and intensity of the contractions is severely reduced. There would seem to be nothing to recommend the wider adoption of this method of obstetric analgesia.

### Local Anæsthesia

This should not really be considered under the heading of anæsthetics applicable to the second stage of labour, but it is mentioned here for convenience. Infiltration of the perineum, with 2 per cent. novocain solution into which a few minims of 1 in 1,000 adrenalin solution have been dropped, forms a reasonably satisfactory preliminary to suture of lacerations. The repair can be rendered almost painless, sufficient time is allowed for careful apposition and healing is usually good.

This form of anæsthetic is of particular value for perineal repair in cases where it is desirable to avoid a general anæsthetic. Examples would be certain medical complications, and more especially if it is wished to avoid the re-induction of anæsthesia, as, for instance, with chloroform. Repetition of this anæsthesia seems to carry a grave risk of delayed chloroform poisoning. Cases to which a general practitioner is called by a midwife who requests that her patient's perineum be repaired constitute another indication for this method of anæsthesia.

### ANÆSTHETICS FOR CÆSAREAN SECTION

Perhaps the ideal for this operation from the viewpoint of the operator is spinal anæsthesia. The abdominal wall is well relaxed and the uterus contracts very vigorously so that hæmorrhage is reduced to a remarkable degree and the child is unaffected. But these advantages are, to our minds, outweighed by the disadvantages. There is a mortality risk attached to spinal anæsthesia which appears to be unavoidable. In a letter to the *B.M.J.* (October 9th, 1937) the late Dr. Herbert Spencer drew attention to the fact that many authorities, including Dr. Lee, Krönig, Brouha, Voron, Winter and Halban, regarded spinal anæsthesia as dangerous in pregnancy and in labour perhaps because of a special bulbar sensibility in these women to the action of cocaine compounds. Whatever be the explanation of the dangers attaching to spinal anæsthesia for pregnant women the fact remains that most obstetricians have a very real fear of this form of anæsthesia for their patients. But from time to time one finds advocates for this method, as for instance, Sebrechts (23), who, while admitting the special susceptibilities of parturient women to spinal anæsthesia, claims that safety lies in a fractional method of administration. In this method he uses percaine in 1 in 1,500 solution. Of this, small doses of 5 c.c. are given at five minute intervals until the desired effect is produced. And though 20 c.c. is stated to be the average dose for a non-pregnant woman (and many anæsthetists would regard this as a remarkably heavy and dangerous dose for anybody), 10 c.c. is said to be the proper dose for a Cæsarean section case. He records 115 cases with no failure but one is tempted to wonder if his 10 c.c. doses will continue to provide immunity to accidents. Other disadvantages that call for brief mention are the facts that the incidence of post-operative headache still remains a serious drawback and, equally important, there is the pain inflicted on the mother during the

actual injection. There is always some unpleasantness for the patient attached to the administration of a spinal anæsthetic even when the operation is facilitated by a well-flexed attitude of the lumbar spine. And this attitude is impossible of attainment by the pregnant woman at term. Therefore the insertion of the needle sometimes becomes a matter of great difficulty even to the expert. During the struggle to overcome such difficulties on the occasions when they are experienced, the woman about to be operated upon is exposed to a degree of discomfort, which we consider indefensible.

Our preference is for one of the inhalation anæsthetics, and we consider that, in order to ensure that the child receives the minimum of anæsthetic, the administration should not be commenced until the patient is on the table with the dressings removed, the skin prepared, and the operator ready to make the incision. Again in the interests of the child no premedication should be permitted. Morphia, the barbiturates and avertin are all dangerous to the fœtus and should be avoided. The induction should be smooth but rapid, and for this purpose gas and oxygen may be used if the services of one skilled in its use are available. The development of cyanosis should not be allowed, but even in its absence it is remarkable how much inspired liquor amnii can be poured out of the child immediately after its extraction when this anæsthetic has been employed.

Eastman's work on the effect of nitrous oxide on the fœtus has already been referred to. He has shown that with strong concentration of  $N_2O$  for periods of more than five minutes there arises a considerable danger of the child being born in a state of grave asphyxia neonatorum. It would in fact appear that, under certain circumstances, the child born of a mother who is receiving nitrous oxide as an anæsthetic, may be born in a state more closely approximating to fatal anoxæmia than is the case with any other anæsthetic.

The occasionally unsatisfactory immediate post-natal condition of some children delivered by Cæsarean section performed under nitrous-oxide-oxygen anæsthesia is thus explained. It is because of this that we prefer the old-fashioned method of induction of anæsthesia by a mixture of chloroform 2 parts and ether 8 parts. Let it again be made clear that this induction is carried out with the surgeon standing by, all ready to make the incision. This anæsthetic can be given by one without special experience in anæsthetics and will yield a smooth and rapid induction, after

which the delivery of the child can speedily be completed. Once the baby is delivered there is no further need for hurry, and a change to open ether gives safe anæsthesia with adequate relaxation.

Admittedly this routine is not pleasant for the mother, but the explanation to her that it is in the interest of the child always secures her co-operation. In order to obviate this unpleasantness, many methods of premedication have been tried. The barbiturates have been used and so has the rectal administration of paraldehyde or of quinine-alcohol-ether oil according to Gwathmey's formula. It appears to be the general opinion that such premedication is inadvisable owing to the added risk to the child and in our view it is contra-indicated.

But if, for some special case, it is intended to perform Cæsarean section under local infiltration anæsthesia some such pre-operative treatment is necessary. For this reason the performance of the operation under this form of anæsthesia is probably unjustifiable except for a case—say of tuberculosis complicating pregnancy—in which the administration of an inhalation anæsthetic would be injudicious.

During recent years cyclopropane has become a favourite anæsthetic for Cæsarean section and, in our as yet limited experience of its use, has many points to recommend it. No question of foetal anoxæmia should arise as so much oxygen has to be used with it. The uterine action is powerful and so the amount of hæmorrhage is less than the usual for cases of Cæsarean section. W. Bourne (24) is among its advocates in America. But it has the disadvantage that it is more than usually difficult of administration and requires the services of a skilled anæsthetist using special apparatus.

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## CHAPTER VI

### PUERPERAL SEPSIS

AMONG the recent advances to be considered under the heading of puerperal sepsis are the following :

(1) The attitude of the ordinary doctor towards the disease, the modern conception of its nature, the clinical types and the appropriate investigations.

(2) The improvement in our knowledge of the bacteriology of the disease.

(3) Improvements in treatment.

#### The Conception of the Nature of the Disease

There has been for many years a strange idea in the minds of our profession whereby they have regarded puerperal sepsis as sometimes being a serious and quite well-understood pathological condition which was called septicæmia. At other times their cases have been described as a weird pathological absurdity called "sapræmia," which in some curious fashion appeared to have been intimately connected with retained products of conception.

This word "sapræmia" is at last disappearing and all of us are realising that puerperal sepsis is wound sepsis just as seen as a result of accidents, or in war. All parturient women have one wound—the placental site—and, therefore, each one has some risk of developing puerperal sepsis. If there are additional wounds, such as cervical or perineal tears, then the risk of infection is proportionately increased.

In the same way if a gunshot wound becomes infected with a virulent hæmolytic streptococcus then the sufferer is in danger of a most severe illness frequently amounting to actual septicæmia. So the recently delivered woman who is unfortunate enough to have had the hæmolytic streptococcus introduced into her genital tract during labour or the first few days of the puerperium is similarly in considerable jeopardy. But if her wounds were infected by organisms of lesser virulence, then she would only become a sufferer from a comparatively mild disease.

What then is the importance of retention of a fragment of placenta or of a large piece of membrane? We know that a piece of placenta retained *in utero* will sooner or later cause post-partum

hæmorrhage. This is a certainty; but such a retained fragment cannot of itself cause infection. This should be obvious to anybody. But somehow the idea that retention of a piece of placenta is followed by puerperal sepsis seems to die so hard that the point must be made clear.

A moment's thought, however, will make one realise that such a retained fragment, though it cannot *cause* sepsis, can *predispose* to it. To understand this we must just consider briefly the protective mechanisation in the uterus itself. When, after labour, the uterus is left empty except for a few relatively avirulent organisms, their presence, by some chemiotactic action causes the arrival of hosts of defensive phagocytes to line the raw surface left as the result of separation of the placenta. The organisms make their attack there and are promptly phagocytosed with, doubtless, the production of a few pus cells but not enough to be noticeable. Some bacterial toxin will also be liberated, but only in such small quantities that its absorption into the woman, gives rise to no symptoms.

Should it have happened that, not a few, but a large number of organisms find themselves occupiers of a recently delivered uterus, there will be a correspondingly greater battle between them and the defending phagocytes. In such a case there will be profuse purulent loss from the uterus and considerable liberation of bacterial toxin, absorption of which into the woman makes her ill. This illness is manifested by a rise of temperature and the appearance of purulent and perhaps offensive lochia. In other words, the case is one of puerperal sepsis.

If we now turn back to the consideration of the first of these two cases, the one in which a very few organisms were promptly destroyed in an empty uterus, we can see how the presence of a piece of placenta would adversely affect the patient's outlook. For if such a fragment were present, some of the organisms might find a way into this foreign body in which there is now no active maternal circulation, and therefore no defending mechanism. Here they multiply unmolested, and in time the few organisms have become a great host. This host can be visualised as advancing towards the maternal tissues and there joining battle with the defending leucocytes. Phagocytosis is on a large scale, liberation of toxin is copious, and the woman is ill. There is, of course, also a purulent discharge consequent upon the death of leucocytes in the process of phagocytosis, and to this is added a further offensive discharge as the result of

liquefaction of the retained placenta. This is due, in part at least, to secondary invasion by non-pathogenic organisms. These are the saprophytes, of which we have heard so much. The part they play is to cause liquefaction of retained placental fragments. They also make the lochia offensive. But they do not make the patient ill.

*Clinically* such a patient will probably have a fairly late onset of symptoms because the organisms in her uterus had to multiply considerably before they were in numbers sufficient to be of pathogenic importance. This delay at the same time gives opportunity for the complete mobilisation of the defensive mechanism. In consequence a patient of this type will tend to have a comparatively mild disease.

It can easily be seen from this argument that in a case of puerperal sepsis the offensive smell of the lochia which the midwife tends to stress so much, can usually be regarded as a sign of hopeful import and not the dreadful thing which she suggests. If, then, retained placenta be relegated to the position of a predisposing cause it will be convenient here to mention briefly the other conditions which may be included under this heading.

### PREDISPOSING CAUSES

Lacerations have already been discussed, and exhaustion of the mother in consequence of a prolonged labour is always regarded with apprehension. Previous debilitating conditions such as anæmia, under-nourishment (in which may possibly be included vitamin deficiency—particularly deficiency in vitamin A) and albuminuria may be mentioned. Certain cases of puerperal sepsis may be "endogenous" or "autogenous." Organisms already present in the woman—such as *B. Welchii*, *B. Coli* and anaerobic streptococci—seize a favourable opportunity to multiply and to become pathogenic to their previously immune host. But the development of the important streptococcal puerperal infection is always due to the implantation of this organism in the genital tract during the course of delivery or in the first few days of the puerperium. We cannot take comfort in the supposition that there is such a thing as endogenous hæmolytic streptococcal infection. Nor that there is even an autogenous infection by these streptococci, except in so far that germs from the patient's own throat, etc., may be assisted towards the placental site during labour. Pathogenic hæmolytic streptococci do not live in the



human vagina except in the rarest of instances. They cannot survive in that acid environment. There can therefore be no endogenous infection; and autogenous infection by hæmolytic streptococci from the bowel is practically excluded, since virulent organisms of this kind are scarcely ever found in the fæces. This subject will receive consideration in greater detail in a later section of this chapter.

Tissue damage is a predisposing cause which needs consideration. We know that anaerobic streptococci are fairly common inhabitants of the vagina of a pregnant woman (White, E. (1)). They are not actively pathogenic and their development into a potential source of danger probably depends on their gaining access to damaged tissues. The normal vagina can keep these organisms in check, but the lacerated, bruised and devitalised tissues after a difficult delivery appear to have a much reduced killing power against these germs. They are able, therefore, in such cases to multiply greatly and to lead to the development of anaerobic streptococcal puerperal sepsis.

At this point it may be as well to define autogenous, endogenous and exogenous puerperal infection. Autogenous infection is one which, present in some other site in the parturient woman, is conveyed to the genital tract during or shortly after delivery. Endogenous infection is an infection by microbes present in the woman's genitalia as a pre-natal occurrence. Exogenous infection is by organisms introduced into the birth canal by some wholly extraneous agency. As an example of the autogenous type may be cited infection of genital tract by *B. coli* which had previously inhabited the patient's urinary system. The best example of endogenous infection is that by anaerobic streptococci in the manner described in the preceding paragraph. Exogenous infection is typified by any serious case which has been infected, as is always so, by hæmolytic streptococci conveyed to the woman from an attendant's throat or from other outside agency such as dust.

### EXCITING CAUSES

The organisms commonly leading to the production of puerperal sepsis and the methods by which they gain access to the genital tract are fully discussed later in this chapter. It is merely necessary here to state that droplet infection from an infected respiratory tract, dust, infection conveyed from contaminated skin or a definite septic focus, endogenous infection (*e.g.*, *B. welchii*),

etc., all come in for further notice. But it is convenient at this point to give brief mention of some of the obstetric activities by which the entry of organisms is facilitated. *Frequent vaginal examinations* or *instrumental delivery* can lead to puerperal sepsis even if the proper precautions are taken against hæmolytic streptococcal infection from the respiratory tract. For by such manœuvres other less virulent organisms may be conveyed into the upper regions of the genital tract in consequence of some failure in aseptic and antiseptic technique. *Manual removal* of the placenta has a very bad reputation as the cause of puerperal sepsis. It is probably by direct conveyance of infection from the lower to the upper genital tract that it produces its ill-effects. The *modus operandi* is obvious from the fact that the hand performing the operation is applied directly to the open mouths of the large venous sinuses. At Queen Charlotte's Hospital, where the operation is done with every possible care, with the gloved hand and liberal use of antiseptics, of 199 patients from whom the placenta was removed manually 42% had a febrile puerperium and 2% died. *Induction of labour* probably acts by a similar conveyance of organisms from the lower to the higher genital tract. It is interesting that although a mild form of sepsis is common after induced labour the mortality rate is no greater than the general rate for sepsis quoted in the Registrar-General's returns. At Queen Charlotte's Hospital of 582 consecutive cases of induction of labour by bougies or introduction of bags there was a morbidity rate of 15%, but only one patient died, a mortality of 0.17%.

One is perhaps permitted to deduce from this that the organisms conveyed inside the uterus from the vagina are of a virulence inferior to that of the organisms sprayed from an ill-masked medical attendant's throat.

*Exploration of the uterus* after labour is now much less common than it used to be. Doctors are learning to restrain themselves from this activity when some evidence of sepsis has appeared. This matter will be referred to further when we come to discuss the subject of the treatment of puerperal sepsis. In the meantime it will be sufficient here to say that no uterus should be explored immediately after delivery unless there is clear evidence of retention of a definite fragment of placenta. And be it remembered that the incidence of retention of a cotyledon of placenta within the uterus is extremely small, possibly about once in one thousand labours.

## Clinical Types of Puerperal Sepsis

1. The simplest type is a *localised wound infection*. The wound may be the placental site, with or without a retained fragment of placenta, or it may be a cervical, vaginal or perineal laceration. The important thing is that the defensive mechanism has been adequate to localise the infection to the wound in question and no deeper spread has been permitted. Clinically, therefore, the patient will be pyrexial, there will be a variable amount of purulent discharge from the uterus (if it be the placental site that is infected) the uterus may be tender, etc. But the proof of the existence of this condition depends upon bacteriological investigation (*vide infra*).

2. There has been a wound infection, but either because the organism is very virulent or because the defensive forces have been inadequate, extension—in this case into the blood-stream—has occurred and *septicæmia* is the result. Clinically this condition will be suspected if there have been one or more rigors, if the temperature is 102° F. or higher, and if the pulse rate is over 120 per minute. These three signs, alone or in combination, at once proclaim that the case is a serious one and strongly suggest a blood-stream infection. But again the proved diagnosis rests upon bacteriological investigation.

3. The infection has again started as a local one, but the defences have been pierced and the organisms have progressed directly through the uterine musculature into the general peritoneal cavity—for the recently delivered uterus is an abdominal organ—with the production of *general peritonitis*. The diagnosis of this condition is difficult, but it is suggested by the presence of marked distension and particularly if there has been a sudden attack of *diarrhœa*. If there be hiccough and tenderness—particularly “release tenderness”—together with some degree of guarding, not amounting to rigidity, the diagnosis is probable. But certainty in this matter of diagnosis is difficult to reach. For it will be recognised that the clinical picture is different from that of classical peritonitis. The question of treatment is referred to when the uses of sulphanilamide and the place occupied by laparotomy, are considered.

4. The infection, at first localised, has eventually spread, this time along the Fallopian tubes. This gives rise to *salpingitis*—or better, *local pelvic peritonitis*, this term signifying a different picture from that of generalised peritonitis. In such cases there may have been fever for several days which, instead of beginning

to fall, now rises to a higher level. At the same time there is lower abdominal or pelvic pain, some slight rigidity and considerable tenderness in the same area. Within a day or two there appears an ill-defined mass in the lower abdomen and the lower part of this mass may be palpable by the vagina. But it is usually not until several days later that the mass has defined itself clearly and now appears to bimanual examination as a bilateral lump postero-lateral to the now fairly well-involved uterus.

5. A similar initial lesion is here followed by spread along the lymphatics with the production of a *cellulitis*. The original infection in such a case may well have been an infected cervical laceration. Perhaps the persistence of pyrexia has suggested that all is not going well and when, say about the fourteenth day of the puerperium, *i.e.*, rather later than in the case of salpingitis, increased fever and the onset of pain calls for pelvic examination, a mass is felt occupying the side and back of one half of the pelvis and pushing the uterus over to the other side. Later the mass may spread, and if so, it rises up over the brim of the pelvis and is felt on abdominal examination in the corresponding iliac fossa. Suppuration may occur and the abscess may point above Poupart's ligament. More rarely it may track through to the buttock. Very exceptionally it extends to the thigh, or to the peri-nephric fossa.

In connection with the formation of these localised lower abdominal and pelvic masses it is frequently difficult to make the diagnosis between salpingitis and cellulitis. Often the two conditions are combined. In any case the differential diagnosis is of little importance for the treatment in each case is the same, *viz.*, bed, hot fomentations or external heat in any other form, internal heat by ultra-short-wave diathermy or the infra-red lamp, etc., analgesics and other palliative measures to increase the patient's comfort and to promote the absorption of the exudate. Any resort to surgery is to be condemned until there has been abscess formation.

6. The initial wound infection has, of course, occurred, but this time the spread has been directly into and along the veins, manifesting itself as a spreading infective *thrombo-phlébitis*. Rapidly spreading friable infected clots will fire into the circulation frequent fragments teeming with organisms. A high swinging temperature with repeated rigors results, and the condition is sometimes called "acute pyæmia." Usually death follows before metastatic abscesses become clinically recognisable. A similar

but slower process is associated with fewer rigors, and generally speaking is a more "chronic pyæmia." The ultimate survival of the patient depends on the localisation of the resulting abscesses and their accessibility to surgery. It may be necessary to deal with joint suppuration, lung abscesses, pan-ophthalmitis or other foci of suppuration. Successful management of these or similar complications may eventually be followed by recovery. A still slower spread of the thrombo-phlebitis results, not in the setting free of embolic particles, but in occlusion of the larger veins, including the internal iliac. This leads to œdema of the thigh and leg, and if there be an associated lymphatic occlusion the typical "white leg" is produced. There is no recent change in the treatment for this.

The above six manifestations of infection may well be called Genital Puerperal Sepsis. There are two other pyrexial conditions in the puerperium which, though not affecting the genital tract, are so clearly puerperal that they must be mentioned here and may be included in the term Extra-genital Puerperal Sepsis.

These are (7) breast infection, and (8) urinary tract infection.

They hardly call for description, but will be mentioned again under the heading "Investigation." Urinary tract infection will also be dealt with when treatment is considered and it may be convenient to mention at this point that though urinary tract infection during pregnancy is usually a pyelitis or pyelo-nephritis, in the puerperium cystitis may be the only feature. This is perhaps in consequence of the frequent need for catheterisation of a bladder already bruised during delivery (see also Chapter IV).

### Investigation

A case of pyrexia in the puerperium should be regarded as puerperal sepsis until this probability is disproved. And in setting out to investigate the cause of any febrile puerperium the above eight varieties of infection must be considered and tested one by one.

1. The first question then is :—Has the patient a local genital tract infection? Such things as the odour of the lochia and the degree of involution of the uterus should be ignored. We must know if there is a pathogenic organism in the genital tract, and if so what is its nature. The immediate action is, therefore, as follows: put the patient in the left lateral position, pass a speculum, take, on an ordinary sterile throat swab, a specimen of

the discharge from as high in the vagina as possible and plate on blood-agar. Other specimens should be taken and sent to an expert bacteriologist for culture, aerobic and anaerobic, and for recognition of the Group of streptococcus, if such be the nature of the infecting organism. But the inoculated plate of blood-agar properly incubated will reveal the characteristic colonies of hæmolytic streptococci in twelve to twenty-four hours if this important infection be present. Should such colonies fail to appear then the case can be regarded with some degree of equanimity. But if they are present it is prudent to regard them as probably being of Group A and to treat the case promptly with sulphanilamide.

2. Has septicæmia occurred? The reasons for suspecting this have been outlined. The proof depends upon obtaining a positive blood culture. For this investigation it is advisable to obtain the services of an expert bacteriologist. He will collect his specimens at a selected time and will immediately inoculate the appropriate culture media.

3, 4, 5 and 6. Has she got peritonitis, salpingitis, cellulitis or thrombo-phlebitis? The diagnosis of these conditions is made on clinical evidence. From the foregoing brief descriptions of the clinical findings (see pp. 96, 97) in these cases it will be clear that abdominal, vaginal and rectal examinations should be made and the legs and thighs inspected.

7. Has a breast abscess or other form of acute mastitis developed? Examine and see.

8. Is there an infection of the urinary tract. Take a catheter specimen of urine and send it to a laboratory for investigation and report. In the meantime examine under the microscope a single uncentrifuged drop from the specimen, for pus cells and motile bacterial rods. The discovery of these in such a specimen would be strong presumptive evidence of a heavy infection by *B. coli*.

To recapitulate :—In addition to the ordinary clinical investigation, a swab from the vagina and a catheter specimen of urine must be examined bacteriologically in all puerperal cases showing a temperature 2° F. in excess of normal, *i.e.*, 100·4° F or higher. If the temperature be 102° F. or more then a blood culture must also be done. These should be part of the standing orders for every resident medical officer with care of obstetric cases.

Should all the investigations directed towards a search for one of the varieties of puerperal sepsis as the explanation of a case of

pyrexia in the puerperium prove negative, then, and then only, is it permissible to look for some other solution. One should never fall into the temptation of ascribing any puerperal rise of temperature to influenza or other prevalent febrile disease until all the possible types of puerperal sepsis have been excluded by the appropriate bacteriological or clinical investigation.

### BACTERIOLOGY

It has been noticed above that puerperal sepsis can be caused only by pathogenic organisms, but that under this heading may be included some relatively avirulent organisms such as *B. coli*, staphylococci, non-hæmolytic streptococci, various diphtheroid organisms, etc. There are also cases in which anaerobic streptococci, frequently a normal inhabitant of the vagina, become pathogenic, probably because of the conditions established when lacerations and tissue damage have rendered those parts of the genital tract a suitable nidus for the growth and multiplication of these microbes. In a similar manner *B. Welchii* from the near-by gut may invade and infect the genital tract if they can there find dead tissue in which they can survive and multiply.

But it is chiefly with the hæmolytic streptococcus that we are concerned. For it is this organism that is responsible for the majority of serious human cases of the disease under consideration. A very great deal of work has been directed against this germ, and research has shown that there are about nine "Groups" of hæmolytic streptococci and that many of the "Groups" are still further divisible into "Types." Dr. L. Colebrook, whose name will be given in frequent references in this chapter, likens the "Groups" to the various nations inhabiting a continent, and the "Types" to the numerous families with minor familial differences one from the other which go to constitute the nation.

The first work on this subject appears to be that of Mrs. Lancefield (2), who in 1923 described five groups of streptococci and designated them A, B, C, D and E. Later, Hare, working at the Isolation Block of Queen Charlotte's Hospital, described some more, and in 1935 Lancefield and Hare (3), whose work had been useful one to the other, published other articles giving further details of their researches.

The present position is as follows. There are about nine groups of hæmolytic streptococci which may thus be listed :—

Group A. This is the all-important Group A hæmolytic streptococcus which is responsible for 90% of all serious streptococcal lesions in man.

Group B. The organism that causes bovine mastitis and is occasionally pathogenic in man.

Group C causes "strangles" in horses and also epidemic puerperal fever in guinea pigs. It has been responsible for a few but serious human cases.

Group D is of fæcal streptococci, some of which are hæmolytic.

Group E is found in various cheeses.

Group F is found in the vagina ante-natally and may possibly be pathogenic at times.

Group G is also found ante-natally and post-natally in the vagina and may occasionally be pathogenic. If so it is always associated with some other organism when causing human infection. With regard to animals, it causes sterility in bitches and can be the cause of septicæmia in dogs and cats.

Groups H and K are not very important, though once at least Group H has been the causative organism in a case of human malignant endocarditis.

The identification of these groups is by means of a precipitin test. Rabbits are inoculated with streptococci of any given group until they produce an immune serum. Streptococci to be tested for their group are killed and an extract is made from their bodies. The serum from a rabbit immunised against Group A will give a precipitate when mixed with the above extract if the organism under test is also Group A. If it does not belong to Group A then no precipitation occurs; and so on for the other groups.

The various Types have been identified largely through the work of Griffith, F. (4) working at the Ministry of Health. He described twenty-three Types from Group A alone, and there are other Types in the other groups but these have not yet been properly worked out. The Types are identified by an agglutination test. This is similar to the precipitin test by which the groups are recognised except that instead of using an extract, dead germs are themselves used. Agglutination occurs and can be recognised macroscopically or microscopically when an emulsion of the bodies of any given type of Group A or other streptococcus is mixed with a serum from a rabbit which has been immunised against that individual type.

What then is the practical upshot of all this? By the ante-



natal examination of specimens from the vagina of a large number of pregnant women Hedley Wright and Taylor (5), in 1930, showed that hæmolytic streptococci were very rarely found at such examinations. On the few occasions when they were discovered, the subsequent course of the case was carefully observed. It was noted that even women harbouring these organisms practically never developed puerperal sepsis. This work was done when investigations on the grouping of streptococci was in its infancy, and it is now probable that the hæmolytic streptococci that were found in occasional cases belonged to Groups B, C and G. As seen above, such groups are but rarely pathogenic to man, and this explains immunity from puerperal sepsis of the women in the vagina of whom these streptococci had been found. It may be accepted that the Group A hæmolytic streptococcus is present in the human vagina before labour only on the rarest of occasions. To what then is this natural immunity of the vagina due? Cruickshank and Sharman (6) demonstrated the correlation of the presence of glycogen in human vagina, and œstrogen in the circulating blood. Thus glycogen is present in the first few days of the neo-natal period consequent upon absorbed œstrogen from the maternal circulation. It is present again from puberty to the menopause, but not after this epoch. When it is present, the normal vaginal secretion is highly acid in reaction and this permits the presence only of acid-resisting organisms. Consequently such organisms as the Doderlein bacillus and similar organisms abound. But pathogenic streptococci find the circumstances present during the reproductive period of a woman's life most inimical to their existence. It may be noted, however, that in the middle months of pregnancy this protective mechanism may be absent or at any rate deficient.

The next step was, therefore, to find exactly what was the cause of Group A streptococcal infection, since autogenous infection had been ruled out. Smith, J. (7), working in the City Laboratory in Aberdeen in 1931, demonstrated the tremendous importance of direct infection from the nose or throat of "carriers." At least 5% of us can be expected to be carriers of hæmolytic streptococci, at least from time to time. Can it therefore be proved that the streptococcus from a given throat caused a given case of puerperal sepsis? Yes. Smith in two groups of cases totalling 40 in all, showed identical streptococci in patient and contact in 39 cases, i.e., 79.6%, the ratio being 31 contact and 8 patients. This identity has been even more abundantly and

conclusively proved by Dora Colebrook (8), and confirmatory evidence has also been supplied by Paine (9) and others. Aggregating the results from these three investigations we get 90 out of 118 cases investigated where there is proof of the identity of the streptococci in the patient's genital tract and in the throat or nose of a contact. Now Group A streptococci do not live in the vagina and uterus during pregnancy. It is, therefore, in the highest degree probable that the transference must have been from the throat of the contact to the genital tract of the patient, and not *vice versa*. We must now accept it as a proved fact that this is the common route of infection in Group A streptococcal cases and we must realise that these and similar pieces of research are the basis upon which the modern conception of the ætiology of puerperal sepsis and all modern efforts at prophylaxis against this infection are grounded.

### Other Sources of Infection

**Skin.** It is doubtful if this is ever of much importance in case of infection by the Group A streptococcus. Colebrook, L., Maxted and Morris-Jones (10) investigated 160 women and tested their perineal and perianal skin for streptococci in the last few weeks of pregnancy. Eleven cases showed hæmolytic streptococci, but none was of Group A. Furthermore, it has been shown that hæmolytic streptococci planted on the skin of the hand disappeared in the course of a few hours. Therefore any such organisms on the hands of an accoucheur are likely to be merely temporary occupants picked up from some other source of infection. But if he possessed a finger wound infected with hæmolytic streptococci such an attendant would of course be virulently dangerous (see below). Apart from this sort of thing the doctor's hands and the patient's perineal skin do not appear to be the source from which Group A streptococci may be expected to emerge as the cause of a case of puerperal sepsis. Other less virulent organisms may thrive in both these situations. From either of these sites they may be conveyed during labour to the upper genital tract and so originate one of the milder varieties of puerperal infection. Such mild cases never give much cause for alarm. It is the Group A hæmolytic streptococcus for which we have a most respectful fear.

**Fæces.** Here again is a possible source of infection with the milder organisms, but it has not often been responsible for infection by the hæmolytic streptococcus. Hare and Maxted (11) examined

the faeces of 100 women in the first stage of labour. Twenty-nine showed the presence of hæmolytic streptococci but none was of Group A. They can, however, exist in the faeces in cases where there is an active streptococcal lesion elsewhere in the patient, for instance, if the respiratory tract be infected or if she be a sufferer from scarlet fever.

**Other Septic Foci.** These undoubtedly cause some cases of streptococcal puerperal fever, but are not responsible for so many as is the respiratory tract. In the series of Smith, 1931 and 1933, there were two such cases, and Dora Colebrook, in 1935, also reported two. In these four cases an identical streptococcus was present in some septic lesion in the patient or a contact, and in the genital tract of the patient. The details are as follows :

In the first, the septic focus was in the patient's own foot ; in the second it was in the patient's own finger ; in the third it was in the finger of the attending doctor ; in the fourth it was in the septic finger of a child in the house in which labour was conducted.

**Dust.** This has also been referred to and undoubtedly can cause infection. The dust of a room in which hæmolytic streptococcal cases have been nursed always contains these germs. Furthermore, they may be able to live for as long as ten weeks. This subject has been carefully investigated by White, E. (12) and Cruikshank (13), and it will be evident that it would be courting disaster to admit a patient during labour or the early days of the puerperium into a room which had recently harboured a streptococcal sepsis case, unless there had been really thorough disinfection.

### Organisms other than the Hæmolytic Streptococcus

**Anaerobic Streptococci.** It has already been stated that these are present in the vagina of 30 to 40% of pregnant women. They can at times lead to puerperal sepsis, but there must necessarily be tissue damage to give lowered local resistance before they are able to exercise pathogenic invasive propensities. Puerperal sepsis cases infected by this organism may thus be regarded as endogenous.

**Bacillus Coli.** This is usually an example of autogenous infection from faecal contamination, urinary spill or conveyance from the perineal skin. The proof that these *B. coli* infections are autogenous has been supplied by Smith, G., who in 13 out of 14 cases investigated, showed serological identity between the *B. coli* in the genital infection and a strain in the urine or faeces.

**Bacillus Welchii.** Infections by this organism are possible only when there is dead tissue present. They are sometimes autogenous by spread from the bowel, but may sometimes be exogenous, having been conveyed on dust. Space does not permit full description of the clinical types of this infection nor the special treatment which it demands, but a very full and detailed account of the disease has been supplied by Hill, A. (14).

**Staphylococci.** These do not often give rise to puerperal sepsis and cases of this infection are usually mild. But the curious paradox is that if this organism does succeed in invading the blood-stream, thereby producing staphylococcal septicæmia, the outlook is almost hopeless.

### Preventive Measures

For a full description of everything that can be done in this direction reference should be made to an article by Colebrook (15). He suggests various administrative reforms, and stresses the necessity for early detection of catarrhal conditions in the respiratory tract due to hæmolytic streptococci. Anybody in obstetric practice who is found to be himself infected should be debarred from attending midwifery cases until the infection has been eliminated. Colebrook does not advise that routine swabbing at regular intervals of all the personnel of the maternity services be carried out. But such an investigation should be performed in the event of any epidemic so that the healthy carriers of hæmolytic streptococci can be detected.

The next step is the early detection of a case infected by these organisms and this matter has already been discussed under the heading of "Investigation." At the same time further swabs should be taken from the mother's own nose and throat, and from the nose and throat of all those who attended her during delivery and the puerperium. Any attendant whose swab gives an abundant culture of these organisms should be suspended from maternity work for the time being.

**The Wearing of Masks.** This is now a generally accepted precautionary measure. It must, however, be emphasised that the masks must be efficient and must not be used as an excuse to keep on obstetric duty any person whose throat is known to be infected. With regard to the efficiency of masks, they must be so constructed as to fulfil the following five principles. They must be thick enough (preferably with an impermeable sheet of material such as paper or cellophane between the gauze layers) to stop any.

high velocity particles projected from the respiratory tract by talking or coughing. They must extend laterally round the face sufficiently far to stop any side blast. They must extend under the chin so as to stop the fall of any low velocity particles on to the accoucher's hands. They must cover the nose as well as the mouth. They must not be worn for longer spells than about four hours and the same mask must not be donned repeatedly. After use they should be discarded by dropping into a bowl containing an antiseptic solution.

**Disinfection of the Hands.** This is an ordinary surgical procedure and the wearing of surgical gloves is now universally accepted as necessary. An additional safety factor is introduced by rubbing over the gloves after application with 30% "Dettol" cream. This is not only highly antiseptic, particularly to hæmolytic streptococci, but retains its antiseptic action for a considerable period of time.

**Disinfection of the Vulval Skin.** Many antiseptics have been used for this purpose but probably the most efficient is again "Dettol" cream. This can be smeared on, and not only produces a reasonable degree of sterility, but also retains its antiseptic powers for some time. It has already been indicated that this antiseptic is more efficient against hæmolytic streptococci than against other organisms, but after all this is the organism which we have most to fear, which produces most of the serious and fatal cases and against which we have most carefully to guard. It should be noted that when the strong "Dettol" cream has been applied to gloves and to the vulval skin frequent swabbing with a weaker solution of "Dettol" is to be deprecated, for these weaker solutions do not offer the prolonged antiseptic effect which is so desirable. Worse, they eliminate the antiseptic effect of the stronger preparation.

**Protection against the Mother infecting Herself.** Ideally, since at least 5% of all of us are carriers of the hæmolytic streptococcus, the parturient woman should also wear a mask. Furthermore, because she often touches the vulva during labour pains, a wise precaution would obviously be to smear her hands also with "Dettol" cream. But it will probably be some time before such measures come into general use.

**The Prophylactic Injection of Anti-streptococcal Serum.** This is almost certainly useless and perhaps harmful. The routine administration of prophylactic sulphanilamide is also to be condemned owing to the occasional production of toxic effects

(*vide infra*). But it may be wise to give this drug after delivery to any woman who has come in contact during her labour with anyone known or suspected to have a respiratory tract infection by the hæmolytic streptococcus.

### Treatment

The proper investigation of any case of pyrexia in the puerperium has already been described. Once a case of puerperal sepsis is diagnosed it should immediately be removed, preferably to a hospital where efficient isolation can be guaranteed. The room the patient had previously occupied must be thoroughly disinfected and the noses and throats of all attendants swabbed.

Once in the hospital good nursing, fresh air and good food play their important part in treatment. Notification is a statutory duty.

**Intra-uterine Glycerine.** This is now not so widely used as previously and its employment is restricted to those cases of local sepsis infected by organisms other than the hæmolytic streptococcus. In cases of streptococcal infection and in cases in which spread has already occurred, the manipulations required in order to give this treatment are likely, by facilitating the spread of infection, to do more harm than good. Even in cases deemed suitable for this therapy the treatment is carried out only for a few days. In cases not suitable, local treatment is restricted to the removal of stitches which may be causing retention of secretions, to occasional vaginal instillation of glycerine or, rarely, low-pressure vaginal irrigation. More usually the local treatment consists merely of repeated changing of soiled dressings.

**Exploration of the Uterus.** This previously popular treatment is heartily to be condemned in the majority of cases. Should there be reason to suspect the retention of *débris*, or even of a piece of placenta, the uterus should be encouraged to expel its contents by the administration of ergot, quinine and pituitarin in the majority of cases. Only if the retained products are causing hæmorrhage, and hæmorrhage of such severity as to be an important feature of the case, is exploration of the uterus permissible. Even then the operation must be restricted to the loosening of any fragment by means of a finger introduced into the uterus and its extraction by sponge forceps. In no circumstances may the curette or the flushing curette be used.

**Blood Transfusion.** Many cases of puerperal sepsis are anæmic either from hæmorrhage at the time of labour or from blood

destruction. Such cases are greatly benefited by blood transfusion. But this treatment does not appear to help in fighting the sepsis itself, and blood transfusion should not be given with this end in view. The blood of the sufferer from puerperal sepsis is very highly bactericidal. The giving of a blood transfusion, including even the "hotted-up" blood of an immunotransfusion, dilutes this bactericidal power and therefore does harm and not good in so far as the struggle against infection is concerned. But again let it be said that it is a valuable treatment for the associated anæmia.

### Chemotherapy

In 1935 Domagk (16) in Germany described the protective influence of prontosil on mice injected with human streptococci. In the same year Levaditi and Vaisman (17), working in France with a similar drug, attained good, but not quite so successful, results in similar experiments. In 1936 Colebrook and Kenny (18) reported other and more detailed experiments on mice, and confirmed the results of Trefouel, Nitti and Rovet (19) which indicated that *p*-amino-benzene-sulphonamide (which we now call sulphanilamide) was the active element in prontosil, or, at least, had a similar protective influence on mice. They also emphasised that repeated doses spread over several days gave better results than did one big one. In the same paper they said that they had the impression that of 38 cases of puerperal fever from hæmolytic streptococci treated by prontosil "in many of the more severe cases the drug has exerted a definitely beneficial effect. . . ." Buttle, Gray and Dora Stephenson (20) also found that sulphanilamide protected mice against streptococci and to some extent against meningococci.

These and other researches first showed that there was a theoretical reason for the use of sulphanilamide and similar substances for cases of hæmolytic streptococcal and some other infections. Furthermore, these theoretical considerations were confirmed by clinical evidence. This last contention is supported by a comparison of the results obtained in the treatment of cases of hæmolytic streptococcal infection admitted to the Isolation Block of Queen Charlotte's Hospital during the years 1931 to 1935, before the sulphanilamide era, and the years 1936 and 1937, when this drug (or prontosil) was used for all severe cases. Generally speaking, prontosil and prontosil soluble were used from January, 1936, until the autumn of that year. Then

sulphanilamide was substituted, but some cases were given prontosil soluble in addition.

TABLE I

*All cases of Haemolytic Streptococcal Infection admitted to the Isolation Block of Queen Charlotte's Hospital*

*Prontosil or Sulphanilamide in routine use during 1936 and 1937*

	No.	Deaths.	Mortality.
1931 . . . . .	98	31	31.6%
1932 . . . . .	90	19	21.0%
1933 . . . . .	97	20	20.6%
1934 . . . . .	120	20	16.6%
1935 . . . . .	90	22	24.4%
	<hr/> 495	<hr/> 112	<hr/> 22.6%
1936 . . . . .	114	5	4.4%
1937 . . . . .	105	7	6.7%
	<hr/> 219	<hr/> 12	<hr/> 5.5%

To resume the story of the development of chemotherapy; prontosil was the original drug and this was followed by a more soluble compound—prontosil soluble. These were complicated compounds and as they had no anti-bacterial power *in vitro* their mode of action was, for some time, a mystery. Then it was shown that they were broken down in the body with the formation of *p*-amino-benzene-sulphonamide and it was easy to demonstrate that this had strong anti-bacterial properties both *in vitro* and *in vivo*. The discovery that a relatively simple compound like *p*-amino-benzene-sulphonamide was a successful chemotherapeutic agent was the beginning of the advances in treatment by the sulphanilamide group of drugs. For chemists were rapidly able to produce many variants of this compound.

Sulphanilamide is now the generally used name for *p*-amino-benzene-sulphonamide and it is marketed under that name by Boots and by Crookes. Bayers calls it Prontosil Album, although it is a much simpler compound than the original Prontosil. Evans, Lescher and Webb call it Streptocide. British Drug Houses and Burroughs, Wellcome & Co. use the name Sulphonamide P.



Such drugs as Proseptasine and Soluseptacine are not of the same chemical constitution and what is said later of the mode of action and the anti-bacterial properties of the sulphanilamide group does not of necessity apply to these two chemicals.

Now as to the variants derived from *p*-amino-benzene-sulphonamide (sulphanilamide). Most of these were either ineffective or toxic but in 1938, Ewins produced *p*-amino-benzene-sulphanido-pyridine, which has come to be known as M. & B. 693, or Sulphapyridine. Contrary to what appears to be the general belief this drug is more toxic than is sulphanilamide. But it is also stronger and has a wider application of use. Thus, Whitby showed that this drug had a powerful curative action on pneumococcal infections which were not benefited by sulphanilamide. And Fleming showed that it acted much more powerfully *in vitro* on streptococci than did sulphanilamide.

Later came the introduction of another derivative, Sulphathiazole, alternative names for which are Thiazamide and M. & B. 760. This acts even more strongly than the other two on streptococci and pneumococci. It also exercises a curative action on staphylococcal infections, though perhaps it is of less value in this respect than was at first hoped. Sulphathiazole is moreover less toxic than the other two and thus it would seem to be a really splendid chemotherapeutic agent. But unfortunately it is rapidly broken down in the body or rapidly eliminated. In any event, it is difficult to keep an adequate concentration in the blood. It is suggested that 10 mgm. per cent. is a blood concentration of sulphanilamide adequate to deal with a moderately severe infection. Such a concentration can be produced in a 10 st. patient by a dose of about 7 gm. of sulphanilamide. But one cannot get this concentration of sulphathiazole without very heavy dosage at frequent intervals—so there are practical difficulties in the use of this otherwise valuable compound.

Still more recently Sulphadiazine or 2-sulphanilamido-pyrimidine has been introduced in America and it is claimed on, what seems good authority (21) that it has properties which may make it superior to any of the other sulphanilamide drugs in the treatment of septic infections. It has, however, not yet been tried to any extent in Great Britain.

**Mode of Action.** There is no doubt that the sulphanilamide group of drugs give markedly beneficial effects in the treatment of infections with streptococcus pyogenes, meningococcus, *B. coli* and gonococcus. Some of them can influence pneumococcal or even

staphylococcal infections. These drugs are mainly although to some extent they are bactericidal, that they act, as has been suggested by Fildes, interfering with the metabolism of the bacterial starved of some substance which is essential for it.

The anti-bacterial action of these chemicals is neutralised by a number of substances such as peptones, bacterial extracts, pus and some chemicals such as *p*-amino-benzoic acid (a constituent of some bacteria).

The fact that the sulphanilamides were essentially bacteriostatic and that therefore the body cells had to complete the destruction of the infecting organisms, led Fleming to suggest that an increase in the immunity of the patient would materially assist the therapeutic action of these drugs. This combined immunotherapy and chemotherapy has been shown to be extremely powerful against experimental infections of mice with staphylococci, pneumococci and the organisms of gas gangrene. But in the field of practical therapeutics the beneficial effect of the combined therapy has not been so clearly demonstrated.

**Dosage.** For cases of puerperal infection the most extensively tried dosage was approximately 1 gm. three times a day for mild cases and twice that amount for more serious ones. This was continued until the temperature fell and then reduced. This would seem to be a wrong principle for two reasons: (a) the serious toxic effects (*vide infra*) appear to follow prolonged dosage even more than they do heavy dosage, and (b) gentle chemotherapeutic attack appears to permit development by the infecting organism of some kind of immunity to these drugs. It is better to attack them fiercely from the first and to avoid prolonging the chemotherapy for too long. Colebrook used to consider that if clinical improvement had not occurred within the first five or six days of treatment, it was unlikely that there would be any response from further treatment. It is possible that he might now shorten his suggested time in view of the risk of agranulocytosis, etc., following the continued administration of these drugs. One might therefore be permitted to suggest a dose of 8 gm. spread over the first twenty-four hours, 6 gm during the next twenty-four hours and 4 gm. on the third and fourth days as an example of what may be administered to a patient with a serious septic infection. An occasional case will be encountered which has an undue susceptibility to these drugs and a feeling of intense illness in the early stages of such a course will arouse

**Suspicious.** A white blood-cell count should at once be done and it may reveal commencing leucopænia. In this event the drugs should at once be stopped. But milder toxic effects may be found only to follow the administration of M. & B. 693, and if this is replaced by the less toxic sulphanilamide, greater tolerance to this chemical may be evident. As to whether it is wiser in routine use to employ sulphanilamide or sulphapyridine (M. & B. 693) for cases of puerperal infection, judgment must be deferred. Clinical trials of sulphanilamide has proved it to be of great value. Sulphapyridine *should* be more powerful. But it is more toxic and sufficient published results are not yet available to justify a final conclusion. As to sulphathiazole, it has not yet received sufficient trial in cases of puerperal sepsis. It may prove of special value for the rare case in which the staphylococcus is the principal infecting agent. Perhaps it may even save the occasional case of that very fatal disease staphylococcal septicæmia.

**Toxic Effects of the Sulphanilamide Drugs.** There is an unfortunate tendency nowadays to overdo the administration of these drugs. Apart from streptococcal puerperal sepsis they are probably of benefit in cases of pyelitis, meningococcal infection, pneumonia, and in gonorrhœa. But their wholesale employment in the treatment of all pyrexial conditions without reference to the nature of the causative organism, and the susceptibility of that organism to the actions of the drugs, is to be deprecated. For many toxic effects have been observed and reported. Perhaps the least important of these is the cyanosis associated with *Sulphæmoglobinæmia* or with *Methæmoglobinæmia*. Cases of this have been reported by Archer and Discombe (22), and by Discombe (28) and others. It is possible that the incidence of this condition may be reduced by not allowing patients at the same time to receive food or drugs, such as eggs, onions and magnesium sulphate, which contain a sulphur radicle, and by keeping the colon empty by enemata. But even should sulphæmoglobinæmia and methæmoglobinæmia appear there is no necessity to discontinue the drug for no great harm seems to result. A common and troublesome toxic effect is a gastro-intestinal upset with vomiting as its main symptom. This is more common with sulphapyridine than with sulphanilamide, but it can occur with any of these compounds. A much more serious complication is *Agranulocytosis*. This is a very grave condition, of which 41 cases had been reported up to August 1st, 1939. Among these, the mortality was over 50%. This high mortality rate appears

to be what may generally be anticipated in cases of this serious complication. The detection of a commencing fall in the white cells is a warning of this danger and so it is, therefore, important to have a leucocyte count done every two or three days on any patient who is taking sulphanilamide for more than four days. Cases have been reported by Jennings and Southwell-Sander (24), by Young (25) and others. That it can occur as the result of the administration of M. & B. 693 as well as after sulphanilamide is shown by cases published by Johnston (36), Sutherland (27) and others. In most cases of agranulocytosis, large doses, in the region of 50 gm., have been given and severe toxic complications have generally followed large doses or the prolonged administration of one or other of the sulphanilamides. But the occasional susceptible case is encountered from time to time in which smaller doses have produced severe and even fatal effects. On one occasion 18 gm. was sufficient to cause death. *Acute Anæmia* appears to be another toxic lesion. Cases of this have been reported by Harvey and Janeway (28) and by Kohn (29). Toxic liver damage and puerperal neuritis following prolonged dosage have also been reported.

Another curious manifestation, apparently a toxic "drug fever," is a sudden *rise of temperature* after it has been normal for some days. The only treatment called for in this case seems to be to stop the administration of the drug. Cases of this type have been reported by Hageman and Blake (30) and by Schwentker and Gelman (31). Other curious toxic symptoms which again respond to treatment by stopping the drug are depression, headache, dizziness, paræsthesiæ and drowsiness. It will be seen, therefore, that the wholesale administration of this drug is not without danger, and the greatest danger, agranulocytosis, though rare, is one of real seriousness.

### Other Treatments

**Vaccines.** These are probably useless in severe cases of puerperal sepsis. The patient is already highly immune. The bactericidal power of her blood is high, the leucocytes show high phagocytic activity and the bacteriotropin response in the serum is good. There may, however, be some value in vaccine therapy for the more chronic localised infections which may persist after the acute attack has been dealt with by sulphanilamide or its derivatives. Combined immuno-therapy and chemo-therapy are at present on trial.

**Anti-sera.** These remarks refer to all varieties of anti-streptococcal serum whether they be polyvalent, anti-scarlatinal or others. Benson and Rankin (82) demonstrated on 114 cases of proved septicaemia that serum was of no value in this condition. Colebrook (83) compared 69 cases treated with anti-streptococcal anti-scarlatinal (anti-toxic) serum before admission to Queen Charlotte's Hospital with other cases not so treated. The treated cases had a mortality of 30.4%, while the mortality in those who had no serum was only 11.6%. In both these groups were many cases that were not infections by the hæmolytic streptococcus.

It is reasonable to presume that at least these were adversely affected by being given another toxin to cope with, namely the serum itself. But if only the cases of hæmolytic streptococcal infection are considered, evidence again points to the probability that the serum did harm. Thus, among these streptococcal cases, the serum-treated ones had a mortality rate of 45%, while those not so treated had a mortality rate of 22.8%. Such figures are not absolute proof, but Colebrook concludes that there is "no trustworthy clinical evidence that the administration of anti-streptococcal serum for the treatment of human infections by hæmolytic streptococci has any specific curative effect." He then goes further and suggests that such administration may sometimes have an unfavourable effect upon these puerperal infections. He excludes from these deductions a possible beneficial effect of injection of sera upon the *toxic* manifestations of scarlet fever. But we must draw the conclusion that treatment of cases of puerperal sepsis with anti-sera must be harmful if the case is not one of hæmolytic streptococcal infection and is probably harmful even in cases that are of this nature.

**Quinine.** Some years ago this had a vogue in the treatment of puerperal sepsis and its administration was associated with a falling temperature. It is now recognised that its curative action is *nil* and its administration by the oral, intramuscular or intravenous routes has been abandoned.

**Metarsenobillon.** This and similar arsenical drugs were given in an extensive trial at Queen Charlotte's Hospital and at one time were thought to have conferred benefit. Further experience, however, demonstrated that this was not the case, and the administration of these drugs has been entirely discontinued here.

**Intravenous Antiseptics.** Perchloride of mercury, eusol, mercurochrome and other drugs have often been given in solution

by intravenous injection in an attempt to cure septicæmia. For years these and other antiseptic substances have been given a more or less extended trial. It is probable that they never have done, and never will do, any good. For their action is primarily against the mother's defensive mechanism, namely her leucocytes, whereby her resistance to infection is diminished. The action of such intravenous antiseptics on the infecting organisms is likely to be of very minor importance. Their administration should therefore, unhesitatingly be condemned.

### Surgical Treatments

Hysterectomy has sometimes been advocated, but it is not called for in cases of local infection, and can only be useless in cases where the infection has spread. There can, therefore, be only very slight scope for this operation. But in certain exceptional cases it may still be called for. Thus it should advisably be performed in cases of rupture of the uterus in a probably infected case; in cases of degenerate and infected fibroids; immediately after Cæsarean section in an infected case, and in the few cases of puerperal fever in which a localised abscess in the uterine wall can be diagnosed.

Laparotomy and Drainage. Before the chemotherapy era this operation had an extensive trial in the treatment of cases diagnosed on clinical grounds as being those of general peritonitis complicating puerperal sepsis. In such cases it appeared probable that beneficial results were obtained. But since the advent of sulphanilamide, all severe cases, including those of suspected peritonitis, have been treated as outlined earlier in this chapter. The results appear to be equally satisfactory, and the operation of laparotomy and drainage has fallen, temporarily at least, into disuse.

Metastatic Abscesses. Incision and drainage of these is such an obviously correct surgical procedure that it needs no further mention here.

Vein Ligature. In general surgery there is the analogous procedure of ligation of the jugular vein for spreading infective thrombo-phlebitis from a lateral sinus thrombosis resulting from mastoid suppuration. In certain cases of puerperal sepsis there is strong reason to suspect a similar process of spreading thrombo-phlebitis. Such a possibility would be suggested by the occurrence of frequent rigors, particularly in a case of anaerobic streptococcal septicæmia with some other associated organisms also in the blood

team. This bacteriological picture has been found to have been so frequently associated with the presence of breaking down infected clot in the pelvic veins, that it may be regarded as a feature strongly suggestive of the diagnosis of spreading infective thrombophlebitis. The difficulty is to pick the cases suitable for vein ligation. If we could be sure that the affected vein was the ovarian, good results could be expected and have indeed been obtained. But effective ligation proximal to a thrombosis of the iliac veins is more difficult. There is usually not one single internal iliac vein on each side but several smaller ones, and their detection, isolation and effective ligation is not easy. At subsequent autopsy it is usual to find that several thrombosed veins have not been tied. The continuance of the pyæmic process after the operation has thus been explained. Cases suitable for vein ligation are, therefore, few and far between, but this operation nevertheless retains its place in the surgery of puerperal sepsis for the few cases in which the proper selection of those suitable for this operation can be made. To be brief, this entails the presentation to the patient of a clinical picture leading to the diagnosis of spreading thrombosis along one or both ovarian veins. That is to say, the bacteriological findings above referred to and which are strongly suggestive of spreading infective thrombophlebitis, plus tenderness and perhaps resistance over the course of one or other ovarian vein.

#### Late Results of Puerperal Fever

A large number of women who had had puerperal sepsis were studied by Kenny, M. (34), who found, perhaps rather surprisingly, that complete restoration to normal health could be expected in the majority of cases. But some troubles did persist in certain cases, and among these, sterility was of considerable importance, together with unpleasant legacies that occasionally manifested themselves as mitral valvular disease and rheumatoid arthritis.

Similar findings were observed in another series of cases investigated by J. B. Barr (35). In addition, he found that an increased incidence of abortion obtained in subsequent pregnancies and a higher incidence of puerperal sepsis complicated subsequent confinements. A further occasional sequel was persistent œdema of one or other leg.

#### Treatment of Urinary Infections

Since it has already been noticed that urinary infection occurring in the puerperium may be included under the term

"extra-genital puerperal sepsis," it is only right that a brief account of the recent changes in the treatment of that condition should be given here. A more detailed account is to be found in the Chapter on "Pyelitis."

The old-fashioned treatment by alkalis is still advised for the acute febrile stage. But if alkalis are to be used they must be used in adequate quantities—say 300 gr. during each of the first few periods of twenty-four hours—and the urine must repeatedly be tested to make sure that it is alkaline and remains alkaline. To obtain this alkaline reaction and to ensure its continuance, at least one large dose of alkali must be given during the night.

Alkalis rarely cause the urine to become sterile, and the first therapeutic measure which really succeeded in bringing this about was the ketogenic diet. In 1933 Fuller and Colebrook (36) published the results of treatment by this method of 54 cases of puerperal infection of the urinary tract. In 24 out of the 54 the urine became sterile within seventeen days. Then Fuller showed that the substance responsible for the success of this treatment was  $\beta$ -hydroxybutyric acid acting in a strongly acid urine. Following along the same ideas, Rosenheim (37) suggested the use of mandelic acid. This treatment being less troublesome and less unpleasant than the ketogenic diet had completely supplanted the latter. The ultimate form of this treatment was to give, not mandelic acid together with substances to make the urine highly acid, but—a simpler matter altogether—ammonium mandelate. A good example of this is the preparation Mandelix (British Drug Houses), which is an elixir of ammonium mandelate of such composition that 2 drachms of the elixir is equivalent to 3 gm. of mandelic acid and 1 gm. of ammonium chloride. This quantity, administered four times in the course of each twenty-four hours, is the accepted dose. Owing to the success of chemotherapy in these cases of urinary infection it is now quite exceptional to have to fall back on treatment by mandelic acid. But should this be necessary in any given case (*vide infra*) the urine must be tested daily with reference to its acid reaction. It must become highly acid—pH 4.5 to 5.0 is to be aimed at. If this be not reached 0.5 gm. capsules of ammonium chloride are also given by the mouth. Fluids should be restricted and exercise encouraged so as to help towards the production of concentrated and highly acid urine. This treatment is apt to produce renal damage, so frequent examination of the urine for casts should be



carried out. If they be found, reduce the ammonium chloride. If they still persist, then stop the treatment.

A simpler and probably more effective method of dealing with puerperal urinary infection is by sulphanilamide and other similar chemicals. It may be wise to treat the initial febrile attack by alkalis, which later are replaced by sulphanilamide when a serious attempt is to be made to kill the infecting organism. That it succeeds in this is shown in Table II, which is slightly modified from Cuthbert's article (38). This table also illustrates the fact that this form of chemotherapy is relatively useless

TABLE II

*Effect of Treatment with Sulphanilamide on Urinary Infections*

Infection	No of cases	Sterile in 7 days	Sterile in 14 days	Bacterial content much reduced	Bacterial content unchanged
<i>B. coli</i> alone . . . . .	37	25	6	3	3
<i>B. coli</i> + other organisms . . . . .	15	3	3	8	1
<i>S. hæmolyticus</i> alone . . . . .	9	6	2	0	1
<i>S. faecalis</i> alone . . . . .	8	0	2	0	6
Other organisms chiefly staphylococci . . . . .	10	3	1	4	2
Total. . . . .	79	37	14	15	13

against cases when the urinary tract is infected with *streptococcus faecalis*. It also fails in some cases of *B. coli* infection. When this is the case the explanation appears to be either that it has been impossible to produce a sufficient concentration of sulphanilamide in the patient's blood and urine or that, perhaps as the result of too low initial dosage, the organisms have acquired a tolerance to these chemicals.

For *S. faecalis* infections and for resistant *B. coli* ones, mandelic acid therapy may be found more useful. But in the great majority of urinary infections the sulphanilamide group is very successful. Even in cases of *streptococcus faecalis* infection, sulphathiazol may prove effective though it has been noted that the other sulphanilamides are useless. For the common case of *B. coli* urinary infection sulphanilamide itself or M. & B. 693 may be used. Sometimes quite small doses have been sufficient. But the risk of small doses being found inadequate and of their having led

to the development of tolerance by the infecting organism, so rendering their elimination a most difficult matter, has led to a tendency to attack these cases more violently from the first. This tendency is shown by a dosage which is sometimes recommended of 8 gm. of sulphanilamide spread over the first twenty-four hours. 6 gm. spread over the next twenty-four hours and 4 gm. during the third day. After this no more should be given and the urine should be sterile. But heavy dosage such as this carries the risk of toxic effects just as much as does a more prolonged course in smaller dosage. It is therefore a wise precaution to have a blood-count done at the end of the first twenty-four hours so as to make sure that there is no appearance of leucopænia. A further blood-count should be done at the termination of the course.

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## CHAPTER VII

### RADIOLOGY IN OBSTETRICS

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#### Introduction

THE increasing use of radiology in obstetrics and the growing appreciation of its value may be regarded as one of the important recent advances.

Obstetric radiology will be considered under four main headings :—

- (i) A study of the foetus *in utero* : normality and abnormality in its posture and presentation, in its growth and development.
- (ii) A study of the maternal pelvis and the foetal-pelvic relationships before and during labour.
- (iii) A study of the soft tissue structures in pregnancy, with especial reference to the placental site.
- (iv) A study of the urinary tract in pregnancy.

In the study of the foetus *in utero*, radiological diagnosis is widely acknowledged as being accurate and the examination causes no inconvenience to the patient. In any case in which there is clinical doubt as to the foetal position, as to skeletal abnormality, as to the number of foetuses present, X-ray examination will usually provide an immediate answer to the problem. The diagnosis of foetal death, however, is not so simple.

In the second group, qualitative and quantitative examinations of the pelvis and foetal head provide interesting information, the value of which, in certain cases, is acknowledged by most obstetricians. A review of obstetric and radiological literature published in recent years leaves little room for doubt that foetal-pelvic relationships and relative proportions and their influence on the prognosis and mechanism of labour are being increasingly studied by radiological methods in conjunction with clinical examination, which must always be regarded as of paramount importance.

Much has yet to be learnt from the examinations in the third group ; it may be said that in selected cases, radiological examination may be of considerable help in determining the placental site.

Before proceeding, it may be stated that there is no danger whatsoever to the foetus in the application of *diagnostic* radiography during pregnancy, providing that multiple extensive abdominal examinations are not undertaken.

### STUDY OF THE FŒTUS IN UTERO

The value of radiology in the diagnosis of multiple pregnancy, of foetal abnormalities such as hydrocephalus, anencephaly, iniencephaly and other gross developmental faults, and of the general posture of the foetus, is so well known, that it seems purposeless to enlarge upon it in this chapter. A few brief observations will be made.

In all cases in which there is hydramnios, radiography should be used to ascertain whether the foetus shows any skeletal abnormality. Hydrocephalus should not be diagnosed on single radiographs ; the distortion and magnification resulting from the distance between the foetal skull and the film must be borne in mind, and skull enlargement should be confirmed in all of three planes, *i.e.*, antero-posterior, postero-anterior and lateral projections.

The finding of abnormal foetal postures should lead one to look for abnormalities of the pelvic inlet, for signs of extra-uterine pregnancy and for such abnormalities as a foetal thyroid tumour if the head is markedly extended.

**Diagnosis of Early Pregnancy.** In very early stages, the diagnosis of pregnancy may be virtually confirmed by hystero-graphy with lipiodol or by pneumoperitoneum. Peterson (1) has shown the enlarged uterus as early as the 6th week by pneumoperitoneum. Both these methods are of academic interest only and have no practical value.

The demonstration of foetal skeletal parts is the most positive confirmatory evidence of pregnancy but in the earlier stages the Friedman test should be used. With good technique, bony foetal parts should be demonstrated at the 16th week, but in some obese patients they may not be appreciated until the 20th week ; in favourable cases they may be seen as early as the 10th to the 12th weeks.

Thus radiographic examination after the 16th week is likely

to provide a rapid and reliable answer to the question as to whether a patient is pregnant. It is of importance to have the pelvi-rectal colon clear of "interference-shadows" due to fæces and gas.

### Extra-Uterine Gestation

The presence of extra-uterine gestation in the later stages of pregnancy may be suspected by the following signs :—

- (i) An absence of the soft-tissue shadow of the uterine wall.
- (ii) An unusual clarity of the foetal skeleton.
- (iii) A considerable overlapping of the bony foetal parts by intestinal gas shadows.

In late pregnancy, when after careful clinical and radiological examination it is still doubtful if extra-uterine gestation is present, it may be justified to perform hystero-graphy.

**Death of Fœtus *in Utero*.** The best known sign of foetal death is Spalding's sign (2), which is an over-riding of the cranial tabular bones due to shrinkage of the cerebrum. The significance of minor degrees of overlapping is not easy to assess and radiographs of the foetal skull in such cases should be taken in two or three planes. Some degree of over-riding may occur in a normal fœtus during enagagement into a relatively small inlet and always occurs during moulding in labour.

With these exceptions, a positive Spalding's sign may be regarded as reliable evidence of foetal death, but the converse certainly does not hold true: *i.e.*, a fœtus may be dead without Spalding's sign being present. Schmitker, Hodges and Whitacre (3) found the sign to be present in only 25 per cent. of dead fœtuses. Roberts (4) found the sign was negative in 50 per cent. of dead fœtuses at the first examination, but advises that weekly control radiographs should be taken. The presence of hydramnios usually prevents the development of Spalding's sign. Matthews has shown that a positive sign may be seen within four to seven days of foetal death, but it usually takes longer to develop.

The status of Spalding's sign is therefore this: a positive sign before the onset of labour is a reliable indication of foetal death: a negative finding does not exclude foetal death. The radiological findings must always be carefully correlated with clinical findings before final acceptance.

Other described appearances of foetal death are not so reliable :—

- (i) Pronounced spinal augulation. Jungman (5) described an accentuation of the lumbo-sacral curve as suggestive, but a

true lateral view of the foetal spine would have to be obtained to estimate this.

(ii) Collapse of the thoracic cage usually occurs only with advanced maceration of the foetus.

(iii) The foetus appears as if rolled up into a ball (Hartley (6)) : this is fairly constant in foetal death but is also seen in numerous normal cases.

(iv) Disparity between the clinical estimate of maturity and the size of the foetal skull. Because the menstrual history is notoriously unreliable any disparity carries little weight.

(v) Continued lack of growth of the foetus as shown by control studies at intervals. This is reliable but not of much practical value.

**Estimation of Foetal Maturity.** The foetal maturity may be judged from :—

(i) The general appearance of the foetus.

(ii) The stage of ossification.

(iii) The size of the foetal skull.

The experienced worker in obstetric radiology using constant technical conditions undoubtedly is able to make a shrewd guess as to the maturity from the general appearance of the foetus ; such a judgment may be useful but is not reliable.

The ossification of the foetal skeleton may serve as a rough guide to foetal maturity, by noting the development of certain centres of ossification. However, superb technical radiographs are essential and these are often unobtainable in cases with hydramnios or marked obesity, which are just the type of case in which the obstetrician may seek help. Apart from this, the accepted dates of appearance of certain ossific centres which are commonly used are mere averages and are subject to variation within wide limits of normality. Reliance certainly cannot be placed on estimates made from the degree of ossification. The centres of ossification which may be useful are :—Cuboid, 40th week ; upper tibia, 40th week ; lower femur, 35/40th week ; astragalus, 24/32nd week ; os calcis, 21/29th week. The writer has seen the lower femoral epiphysis clearly ossified in both lower limbs as early as the 24/25th week.

An estimate of the foetal maturity is often made by measurement of the foetal head, *i.e.*, cephalometry, which is discussed more fully in a later section. Different workers aim primarily at measuring a certain diameter (or more than one), either the occipito-frontal, the suboccipito-bregmatic or the biparietal. In

selected cases, an accurate measurement may be possible: in most cases, only an approximate measurement is feasible: when the measurement has been made, recourse is made to such work as the combined equation graph of Scammon and Calkins (7) which gives the *average* size of the occipito-frontal diameter in relation to the maturity; the graph also indicates the upper and lower limits of normal variation. For example, with a corrected occipito-frontal diameter of 11.0 cm., the average maturity is thirty-six weeks, but the maximum for this measurement is forty weeks, and the minimum is thirty-two weeks. Thus in the later stages of pregnancy there may be a plus or minus error of no less than four weeks compared to the average. These limits are admittedly exceptional, but in practice, even with accurate measurement, one should allow a four-weeks overall variation in an estimate of maturity, and a report should state that though the estimate is  $x$  weeks, the actual age may well be " $x + 2$ " weeks or " $x - 2$ " weeks. Reece (8) estimates the biparietal diameter and works on the assumption that this increases by 0.1 inch per week from thirty weeks to full term.

Thus an estimation of foetal maturity cannot be regarded as an accurate or reliable procedure even though the head measurement may be accurate. As Roberts (9) puts it, "in any case of clinical doubt as to maturity, such methods (cephalometry) are, however, justifiable as being the only alternative means at our disposal."

## RADIOLOGICAL STUDY OF THE MATERNAL PELVIS AND FŒTAL-PELVIC RELATIONSHIPS

**Introduction.** The evolution of radiological study of the pelvis in obstetrics makes interesting reading and has produced a considerable literature, much of which is concerned with radiological technique and less with a critical appraisal of the value of the study. Until comparatively recently, obstetricians and radiologists have approached this study from their own particular angles and hence there has been misunderstanding and an inadequate use has been made of X-ray examination. In recent years, however, it is evident that there has been more co-operation and radiologists have come to appreciate the obstetrician's viewpoint, and *vice versa*. No investigation in medicine employing an ancillary method gains more from the co-operation of the specialists concerned than this study of the pelvis.

In earlier years, the main work was concerned with measurement of the pelvis—*pelvimetry*—and the inlet claimed most



attention. Then interest was widened and the dimensions of the outlet were studied and finally the pelvis as a whole could be measured with a high degree of accuracy. It was gradually appreciated that except in marked degrees of pelvic contraction with inevitable absolute disproportion, the shape and form of the pelvis as a whole in its various planes was as significant as the mere size of certain diameters. This essentially qualitative study owes much to the work of Caldwell, Moloy and their colleagues.

We thus arrive at the study of shape and form, termed *pelvioradiography* by Caldwell (10), and the study of measurement (pelvimetry) of the maternal pelvis linked up with the measurement of the foetal head (cephalometry). Obviously pelvioradiography, pelvimetry and cephalometry cannot be considered separately: they are complementary methods leading to the same fundamental aim, namely: is there any likelihood of normal labour being disturbed by variations of size and shape, and how will the mechanism of labour be influenced by significant variations? Can radiology give any information that clinical examination does not? The answer in certain cases is "yes": but even when the clinical outlook appears clear and simple, it is sometimes advantageous for the obstetrician to seek the help of his radiological colleagues.

### Pelvimetry and Cephalometry

The number of different described techniques is legion, and some of these will be considered briefly. It is better to regard the various methods and techniques as individual modifications of basic principal methods.

Tele-radiographic methods (radiography at a long tube-film distance to minimise magnification and distortion as is used in modern chest radiography as a routine) are theoretically ideal but are impracticable and are therefore scarcely used. The two basic methods in widest use are:

(i) Position methods.

(ii) Stereoscopic and triangulation methods.

**Position Methods.** Many of the described techniques use the semi-sitting position described by Albert (11) in which the plane of the pelvic inlet is so arranged as to be parallel to the film. The patient is seated on the Potter-Bucky diaphragm or stationary grid with the back inclining against a rest usually set at an angle of about 55 degrees to the horizontal for an average case. The upper margin of the symphysis pubis and the spinous process of

the fourth lumbar vertebra are identified by palpation and brought to the same horizontal level: this may be checked by calipers carrying a spirit level. The tube is centered vertically above the centre of the inlet: thus a supero-inferior view of the pelvis is obtained. True lateral views are also included in most of the techniques to be described.

The different modifications are not usually positional but variations in the method of correcting magnification, and some of the best known are described under their authors' names.

*Thoms (12). Pelvimetry.* Supero-inferior (Albert) and lateral views. The radiograph of the pelvis is taken and the patient is removed, leaving the tube and film undisturbed. An opaque sheet of metal in which small holes have been punched at regular 1.0 cm. intervals (longitudinally and transversely) is then placed in the same plane above the film that the inlet occupied. A flash exposure is made through this grid on to the film. The resultant radiograph shows the inlet outline with regularly-spaced black dots which will be rather more than 1.0 cm. apart. The number of dots overlying a diameter (allowing for obliquity) will represent directly the true measurement of this diameter.

*Cephalometry.* The supine position is used and after clinical palpation, the tube is centered vertically above the mid-point of the long axis of the foetal head: the perforated grid is applied as in pelvimetry.

*Walton (13). Pelvimetry.* Positions as in Thoms' method. Correction is made by a "false-centimetre-chart," prepared by radiographing test-objects at a standard focus film distance. The chart, once made, may be used for all cases radiographed at this standard distance. *Cephalometry.* The foetal head is radiographed in two planes at right angles and the "false-centimetre-chart" is applied to correct the measured occipito-frontal diameter and biparietal diameter.

*Roberts (14). Pelvimetry.* Positions as in Thoms' method: the correction is applied by a simple arithmetical calculation. The true diameter equals the false diameter  $\times$  a correction-factor (which is less than unity). This correction-factor, usually of the order of 0.8, is the focus-inlet distance divided by the focus-film distance. If a standard focus-film distance is used, then all the corrections may be tabulated or put into graph form and applied to all future cases. *Cephalometry.* Roberts uses an approximate method. The patient lies prone with the immediate supra-pubic region (in vertex presentations) as close as possible to the film.

A variable correction-factor is applied depending whether hypogastric contact with the film is good or bad. The method is based on Reece's work (8) of measuring the diameter of the greatest circular section.

*Rowden (15). Pelvimetry.* With the same basic position (Albert) a longer focus-film distance than usual is used. During the exposure, the symphyseal region is shaded by an opaque mask to prevent over-exposure anteriorly. Correction is made by one of a series of previously prepared "pubic scales," each appropriate for a certain distance of the inlet plane above the film.

*Courtney Gage (16).* The same basic position is used. A corrected charted outline of the inlet is prepared from the radiograph by reconstructing the actual technical "set-up" used during the radiographic exposure. This reduced tracing or chart shows not only the true size but also the corrected shape of the inlet, and is of especial value in asymmetrical pelves and for teaching purposes. The original description of this method by Dr. Gage was given in earlier editions of this book: as it has not been published in its original form elsewhere, it is given fully in an appendix at the end of this chapter.

Both Rowden's and Gage's methods may be applied to cephalometry by either localisation of the head by radiography in two planes or by clinical palpation.

*Jacobs (17).* This author first estimates the inclination of the pelvic inlet to the horizontal by an instrumental clinical examination using his inclinometer. A supine supero-inferior view of the inlet is obtained: the tube is angled so that the central ray will be at right angles to the plane of the inlet and the film placed so that it lies parallel to the inlet. The necessary angulation of tube and film is known from the first manoeuvre, *i.e.*, estimation of inlet inclination. A lateral view is also used. Jacobs believes that this arrangement is more accurate than the Albert position, because the external conjugate diameter does not necessarily coincide with the true conjugate plane. Correction is applied by Thoms' perforated grid.

*Ball (18).* This worker has a rather original approach. His method is "positional" in character but Hodges considers that its basic principle depends upon "90° triangulation." Ball takes two radiographs, an antero-posterior supine and a lateral. He sets out to compare the calculated volume of the foetal skull with the volume capacity of different planes of the pelvis, giving especial attention to the volume capacity of the inlet and inter-

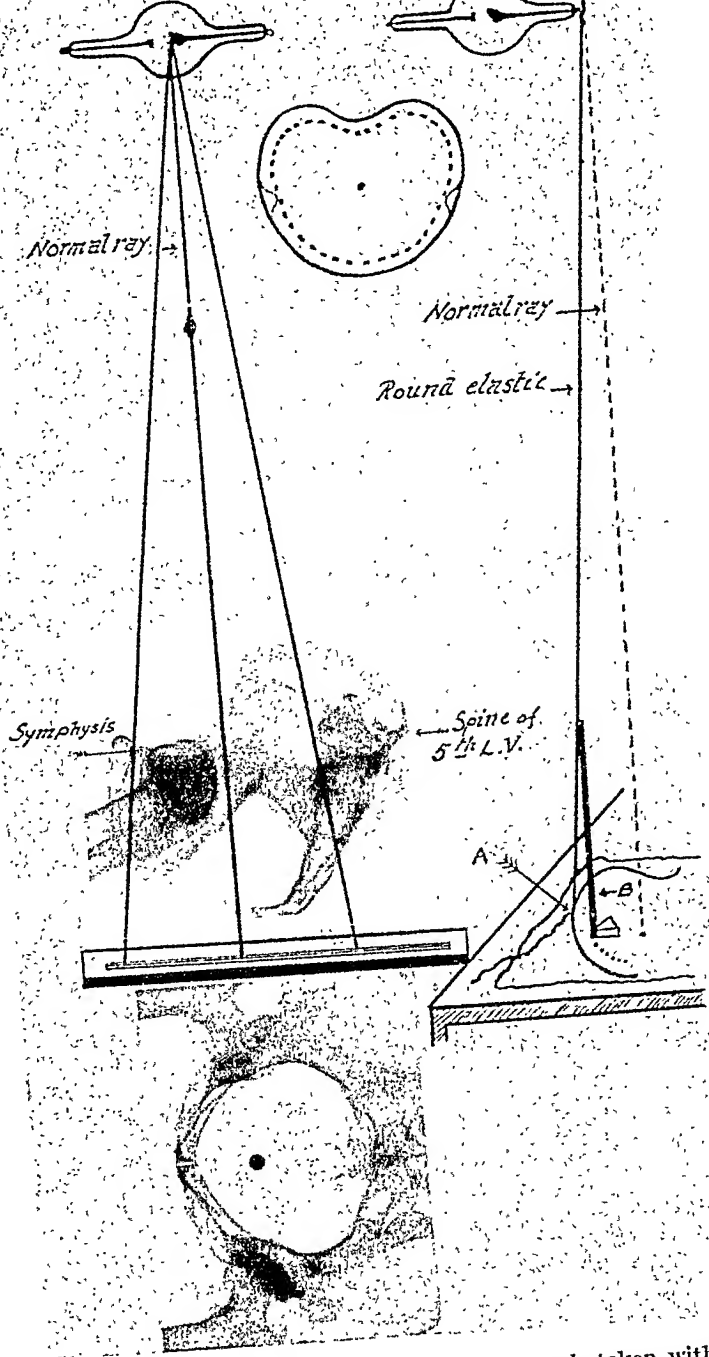


FIG. 12. The pelvis as it appears in a radiograph taken with the tube centred over the pelvic inlet. The black dot indicating the point of incidence of the normal ray.



FIG 13. Breech with extended legs

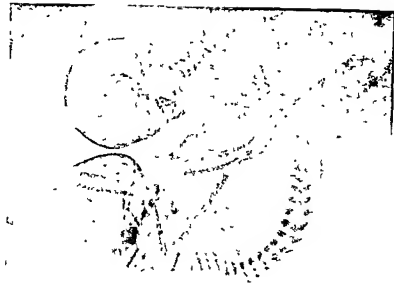


FIG 14. Twins, both breech, internal view.

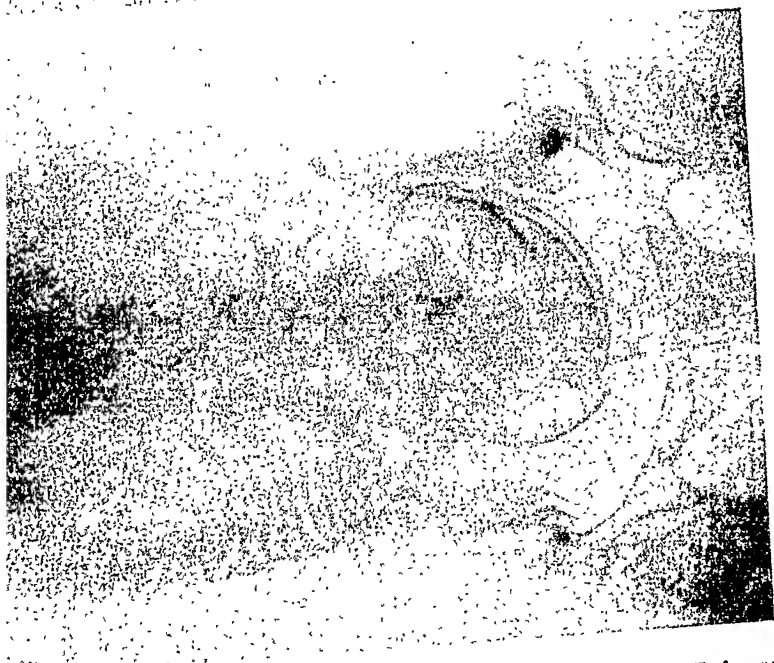


Fig. 15. Dead fetus, positive Spalding's sign.

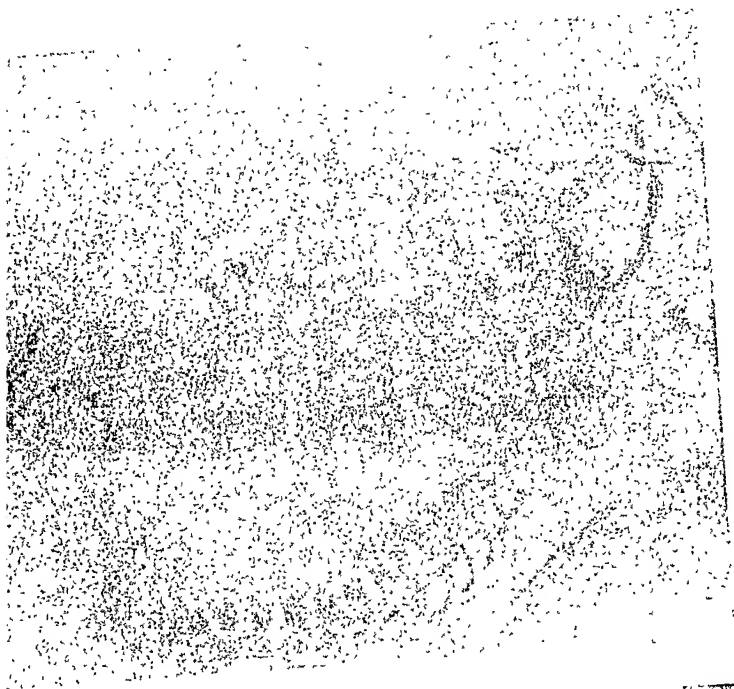


Fig. 16. Anencephaly.



FIG. 17. Android pelvis, inlet view.



FIG. 18. Gunwald pelvis, inlet view.

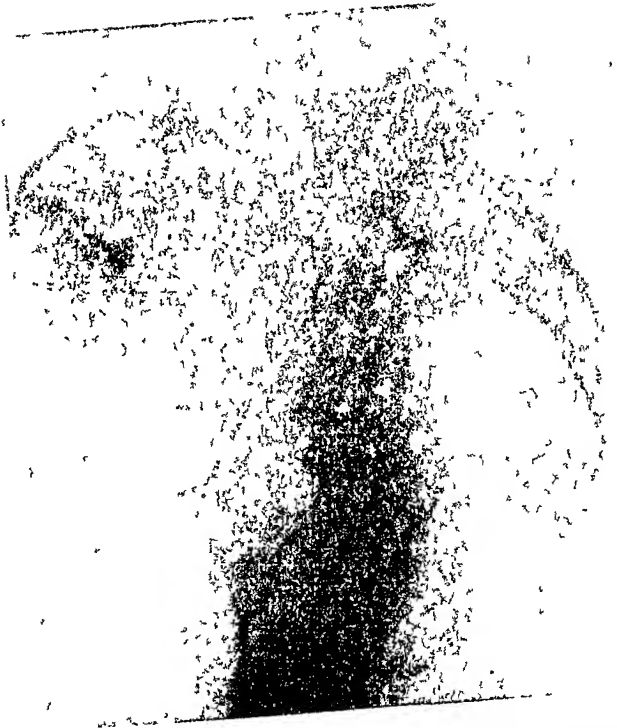


FIG. 19. Lateral view, conjugate diameter marked.

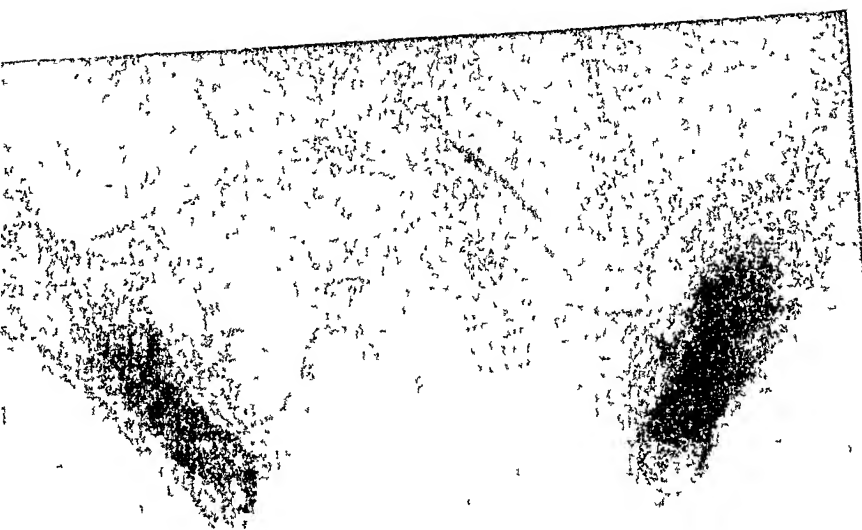


FIG. 20. Outlet view, narrow subpubic arch.

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(i) Lateral view.

(ii) Patient supine, X-ray beam angled at 45 degrees to film, inclined towards the patient's head and centered at the lower margin of the symphysis pubis (one of the positions used by Caldwell and Moloy).

(iii) Patient prone, X-ray beam angled at 60 degrees to the film, inclined towards the feet, centered at the upper margin of the symphysis (used by Hodges).

(iv) Patient sitting on the film, leaning well forward with the abdomen between the thighs: tube centered vertically above the ischial tuberosities (Chassard and Lapiné (21)).

### Anatomical Features seen in the different Projections

An *antero-posterior supine* radiograph of the whole pelvis centered at the upper margin of the symphysis will give a good general survey of the pelvis and will especially show the convergence, straightness or divergence of the side walls. The *supero-inferior* view (semi-sitting position of Albert) will provide an excellent appreciation of the inlet and the dimensions of the conjugate, transverse and oblique diameters. The promontory is not always easily defined, especially in advanced pregnancy, and hence more reliance may be placed on the true lateral view for the measurement of the conjugate diameter. This view also shows the ischial spines and the important inter-spinous diameter can be measured.

The *true lateral* view will show the true and diagonal conjugate diameters, the "obstetric triangle" described by Jacobs (17), and the pubo-sacral or antero-posterior diameter of the outlet. It will also show the shape and inclination of the sacrum and the width of the sacro-sciatic notch.

The various technical methods outlined each have their peculiar advantages and disadvantages. It will be obvious that no single method has come to be regarded as standard; there have been different views as to what information should be sought, to say nothing of the variety of technical modifications to enable one to gain such information.

### THE WORK OF CALDWELL AND HIS COLLEAGUES ON THE OBSTETRIC PELVIS

Introduction. Caldwell and his colleagues Moloy, D'Esopo and Swenson have undoubtedly done a great service to the present

and future conduct and teaching of obstetric practice. Their work has gone far beyond the establishment of a mere classification of pelvic types; it has broadened our ideas and concepts about the mechanism of labour away from the somewhat narrow textbook teachings.

These workers began their studies with an investigation into the influence of pelvic size and shape on the mechanism of labour, because it was clear to them from their experience that many cases of difficult labour were due to pelvic anatomical variations which had received but slight recognition and had been accredited with even less significance.

Whilst many radiologists and a few obstetricians were enthusiastically perfecting pelvic measurement—a quantitative study—Caldwell and his colleagues began to evaluate qualitative pelvic studies—studies of the shape and form of the pelvis in its various planes. Their methods incidentally provided them with quantitative measurements by the ingenious measurement of the “phantom image” using the precision stereoscope perfected by Moley.

Because of the importance of this work, it is hoped in this section to give a reasonable analysis of their researches up to the present time. The writer feels that these researches will have a considerable influence on the practice and teaching of obstetrics during the next few years.

Their work began with studies of pelvises from museum collections and then in post-natal cases in whom there had been difficult labours. They then applied “pelvioradiography” to antenatal cases and have studied the mechanism of labour during labour in well over 1,000 cases both with normal and operative deliveries.

### Technique of Pelvioradiography

Whilst ordinary stereoscopic methods were found to be adequate for a study of pelvic shape, they were difficult to apply to accurate measurement. A precision stereoscope was devised so that the “phantom image” of the pelvis and foetal head could be directly measured in front of the observer through half-platinized mirrors whilst viewing stereoscopic films in pairs.

The following projections are used.—

1 (A and B). Stereoscopic antero-posterior pair of radiographs with the patient supine: a pad is placed under the lumbo-sacral hollow to decrease the pelvic inlet inclination to the horizontal.

The tube is centered vertically above the mid-point of the line joining the anterior superior iliac spines.

2. Forty-five degrees antero-posterior view, patient supine, with the tube tilted towards the head, centering at the lower margin of the symphysis. This is taken for a study of the subpubic arch.

3. True lateral view centering over the sacro-sciatic notch.

### Morphological Classification of Pelves

Caldwell and his colleagues recognise four parent types of pelvis with many intermediate variations in form. These parent forms were the long narrow oval pelvis, the round pelvis, the flat pelvis and the wedge-shaped pelvis and were respectively given the following names:—

- (1) Anthropoid. (2) Gynæcoid. (3) Flat (or Platypelloid).  
(4) Android.

**Description of Parent Types.** (See Fig. 1, p. 15).

1. **Anthropoid Pelvis.** This is a human pelvis resembling that of the higher female apes; it is also called the "transversely contracted" and the "assimilation pelvis." The antero-posterior diameter is long, and the transverse diameter is relatively (or absolutely) short. The fore pelvis may be average or narrow. The widest transverse diameter at the inlet is well forward and hence there is a wide sacro-sciatic notch. The sacrum is long and narrow and may have six segments. The subpubic angle is usually average or wide and the inclination of the inlet is very steep, *i.e.*, in the supine position it is almost horizontal.

2. **Gynæcoid Pelvis.** This is a well-curved rounded pelvis with an average ratio of conjugate to transverse of 11 to 13. The widest transverse diameter is well forward and the fore pelvis wide and smooth. The sacro-sciatic notch is average to wide and the sacrum slopes backwards. The subpubic arch is wide and the side walls are straight.

3. **The Flat or Platypelloid Pelvis.** The A-P diameter is short and the transverse long. The widest transverse diameter is midway between the promontory and the symphysis. The sacro-sciatic notch is small. The subpubic arch and outlet usually conform to the gynæcoid shape but there may be appreciable convergence of the side walls in less typical cases.

4. **The Android Pelvis.** This is typically wedge-shaped, the apex of the wedge at the symphysis. The widest transverse

diameter is near the promontory, the posterior segment of the pelvis being short and the anterior segment long, narrow and angulated. The sacrosciatic notch is narrow, the side walls convergent and the subpubic arch narrow. The public rami are strong and thick and the pelvic cavity is deep.

**Boderline and Mixed Pelvic Types.** Relatively few pelvis conform to a pure parent type. Classification is facilitated by considering firstly the shape of the posterior segment at the inlet, *i.e.*, the segment behind the widest transverse diameter, and secondly, the shape of the anterior segment, in front of the transverse diameter. Thus the term "android-gynæcoid" pelvis refers to a pelvis with a short masculine form of posterior pelvis but with a well-curved wide fore-pelvis.

**The Cavity and Outlet.** Below the inlet, the shape of the pelvic cavity may change as the outlet is approached by variations in the plane of the side walls, of the symphysis and of the sacrum. The transverse capacity of the outlet will be diminished by convergent side walls and long ischial spines. The subpubic arch may be narrow, average or wide but does not necessarily follow the degree of side wall convergence; thus a wide transverse inter-tuberous diameter may be associated with a narrow arch. Further the subpubic arch does not always conform to the shape of the fore pelvis at the inlet level.

Just as the capacity of the fore-pelvis is influenced by the shape of the subpubic arch and the rami, so is the posterior pelvic capacity influenced by the transverse and longitudinal curvature of the sacrum and by its inclination. The relationships of the lower sacral segments and associated ligaments to the ischial spines is of considerable practical importance.

All these various anatomical variations can be judged with a reasonable degree of accuracy by competent clinical examination. The finding of some significant variation at ante-natal examination justifies a full radiological study as a confirmatory measure and as an aid to the obstetrician in deciding the best mode of delivery in difficult cases.

### Summary of the Classification and Description of the Pelvis

The pelvis is first classified mainly on its inlet characters: this is followed by a description of the cavity and outlet and finally measurements of significance are recorded by measurement of the phantom image.

The following scheme is suggested:—

## A. Classification and Description of Inlet Shape

- (i) Anthropoid type (parent)—large, average or small.\*
- (ii) Mixed anthropoid—gynæcoid type.
- (iii) Gynæcoid type (parent).
- (iv) Mixed gynæcoid—flat type.
- (v) Flat type (parent).
- (vi) Android type (parent).
- (vii) Mixed android types: android-anthropoid: android-gynæcoid, android-flat.
- (viii) Asymmetrical pelves.
- (ix) Frankly pathological pelves, secondary to rickets, hip joint diseases, old poliomyelitis, etc.

## B. Description of the Lower Pelvic Zones

- (i) Subpubic arch—wide, moderate or narrow.
- (ii) Pubic rami—straight or curved, slender or heavy.
- (iii) Splay of side walls—convergent, straight or divergent.
- (iv) Fore pelvis—well formed or funnel-shaped.
- (v) Ischial spines—long and narrow, or flat and broad.
- (vi) Sacro-sciatic notch—wide, average or narrow.
- (vii) Sacrum—length, width, inclination, curvature, number of segments.
- (viii) Lateral bore—straight, convergent or divergent.
- (ix) Shape of outlet in front of sacral tip.

**Frequency of Pelvic Type.** In a series of 215 obstetric patients of both white and negro stock, the following percentages of the different types were found :—

Anthropoid	..	22.7%	Gynæcoid	..	..	50.6%
Flat	..	4.4%	Android	..	..	22.4%
		Asymmetrical	..	1.8%		

**Average Measurements in Different Types.** The following figures in centimetres were taken from a series of white patients only :—

Type				Conjugate (cms.)	Transverse (cms.).
Gynæcoid	...	.	..	10.8	13.7
Android	..	..	.	10.5	13.5
Anthropoid	...	...		11.7	12.9
Flat	...	...	...	8.5	14.4
Average for all types				10.0	13.5

\* The terms large, average or small are applied appropriately throughout all the various forms.

These figures well illustrate the poor impression of inlet shape that is given by mere measurement of the important diameters ; it will be seen that the average diameters for the gynæcoid and android types are very similar, whilst their shapes are markedly dissimilar.

### The Mechanism of Labour in Relation to Pelvic Type

The following observations are based on stereoscopic investigation of more than 1,000 cases during the course of labour, observing the descent, flexion, moulding and rotation of the head in relation to the pelvic architecture and the pelvic soft tissues.

**The Head Position at the Onset of Labour.** The head tends to engage with its long diameter in the largest pelvic diameter ; this may be appreciated in the following table based on a series of 200 cases, the figures being given in percentages.

Pelvic Type.			Posterior oblique.	Transverse.	Anterior oblique.	Direct anterior.
Anthropoid	...	...	28.5	37.5	17.0	17.0
Gynæcoid	...	...	10.0	69.0	20.0	1.0
Android	...	...	20.5	71.0	8.5	0
Average for all cases	...	...	18.5	60.0	16.0	0

**Mechanism common to all Pelvic Types.** In most cases engagement begins with the head showing a moderate degree of asynclitism or showing a tendency to a posterior parietal presentation. Synclitism was not observed. The posterior parietal bone overhangs the inlet with the sagittal suture directed downwards and forwards. The anterior parietal bone descends behind the symphysis in a downward and backward direction ; this is largely controlled by the soft tissues of the lower uterine segment.

Apart from the dynamic uterine forces, there are three important controlling factors :—

(i) Flexion and moulding where the head encounters resistance from bone or soft tissues.

(ii) Changes which occur in the long axis of the head as it is forced down and guided through a certain axis in the pelvis.

(iii) Position of this axis of descent : this may be less commonly in the anterior pelvis, or more commonly in the posterior pelvis.

The shape of the pelvic segment through which the head

descends is certainly significant, but the soft tissues of the lower uterine segment have an important influence. In the majority of normal labours, the head will descend in a posterior pelvic axis, *i.e.*, in the most ample part of the cavity. At the bottom of the posterior pelvis, anterior rotation from the transverse or occiput-posterior positions begins and is completed when the head is pushed downwards and forwards to a lower level in the outlet itself. It is possible for normal labour to occur through an anterior axis of descent but this is the exception rather than the rule. It appears to be almost impossible to anticipate the position of the axis of descent, whether anterior or posterior.

### Head Adaptation to Pelvic Shape

Whilst there are exceptions, generally speaking the head positions will be mainly controlled by the shape of the axis through which the head descends.

In the gynæcoid, flat and android types if the head is brought close enough to the sacral region, a transverse position of the head will be favoured. In the anthropoid type, the transversely narrowed inlet with a deep sacral concavity admits the head in the oblique, anterior or posterior positions.

**Deep Arrest.** The influence of pelvic shape on head adaptation is important in the causation of deep transverse and deep posterior arrests of the head. Deep transverse arrest is characteristically associated with a flattened posterior segment in the gynæcoid, android or flat types, whilst the arrested posterior position is typically associated with the anthropoid type when descent occurs through the posterior pelvis.

### Significance of Pelvic Shape in Treatment of Arrest

If a full appreciation of pelvic type and foetal-pelvic relationships is gained during labour, useful suggestions may be made for correct axis of traction, correct level for rotation and the best mechanism through the lower pelvis. At the Sloane Hospital for women, an application of these principles has resulted in, firstly, a lessening in the number of difficult forceps cases without an increase in the number of Cæsarian sections, and, secondly, a decrease in foetal mortality because forceps have been handled on better mechanical principles.

Caldwell and his colleagues make many suggestions as to the manner in which forceps should be applied and as to the level at which rotations should be undertaken. They also advise a

careful consideration of outlet shape before embarking on mechanical delivery.

A list of their published papers is given below :—

- CALDWELL and MOLOY. *Science*, 1932, 76, 37.  
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### CRITICAL APPRAISAL OF THE VALUE OF RADIOLOGICAL EXAMINATION

The value of radiological study of the foetus *in utero* primarily is unquestioned, and need receive no further attention here. However, the status and value of pelvimetry, cephalometry and of qualitative studies of the pelvis and foetal-pelvic relationships is not so clear.

Whatever may be advocated in this essay to urge a wider use of X-ray examination, it must be clearly understood that clinical examination is of paramount and peerless importance, and that radiological study must always be secondary to clinical examination. If clinical methods were perfect, however, there would be no need for radiographic examination. A study of maternal and foetal mortality shows that clinical methods are not always adequate. A short quotation from Fitzgibbon (22) is apt at this point: "At the present time the number of women treated by induction of labour and Cæsarean section is greater than the number of women who suffered from dystocia before the perfection and adaptation of these methods of treatment, but the number of craniotomies, difficult deliveries and disastrous results of delivery with forceps, is not diminished . . . It suggests that the application of operative interference for the purpose of avoiding dystocia is not wholly confined to cases calling for such treatment while it is undoubtedly not applied to many cases in which it would benefit."

It seems clear that the use of any ancillary method by which the obstetrician may improve his judgment is certainly justified.



The value of radiological examination and opinion will surely be enhanced if it receives more constructive criticism from obstetricians than has been the general custom.

What can the radiologist offer to the obstetrician? Firstly, concerning pelvimetry, which in careful hands is accurate; obviously an exact knowledge of certain pelvic diameters is of considerable value. Secondly, concerning cephalometry which is only accurate in cases in which the essential diameters are clearly shown; often a mere approximation of the size of the foetal head only is aimed at or realised. Measurement of the foetal head is not as important as pelvimetry, hence this relative inaccuracy is not a serious adverse factor. The pelvis is virtually fixed in shape and size, but the position of the foetal head may be changed by movement of the foetus as a whole, by rotation about its long or transverse axis (the latter producing flexion and extension) and its shape be changed by moulding. Even if accurate cephalometry is feasible in a given case, if moulding is marked during labour, the accurate measurement seems rather pointless. Hence pelvimetry is of much greater importance than cephalometry.

But there are limitations as to the value even of accurate pelvimetry. Normal unaided labour sometimes occurs when one or more of the measured pelvic diameters indicates that normal labour would be impossible—quite apart from a consideration of the uterine forces which obviously cannot be assessed by radiological means. In such pelves there must be compensatory capacities to permit normal labour when certain diameters seem to indicate absolute disproportion. These compensatory capacities have been well emphasised in the writings of Caldwell and his colleagues who have brought a fuller recognition of the importance of shape and form of the maternal pelvis.

It is thus logical to suggest that the value of pelvic mensuration will be enhanced by a full knowledge of pelvic capacities in all planes. Caldwell's work and the volumetric estimations of Ball (18) represent distinct advances in the endeavour to assess the proportionate sizes of foetal head and pelvic cavity.

After appropriate radiological examination, the wisest course would appear to be to assess obstetric cases into one of three groups:—

- (i) No suggestion of any bony disproportion—the largest group in practice.
- (ii) Borderline cases.
- (iii) Absolute disproportion—the smallest group.

Any arrest in Group I cases will be presumably due to factors other than bony disproportion, *e.g.* poor uterine forces, soft part resistance and unfavourable position of the head. In Group II, the borderline cases, the position of the head and its mouldability are of great importance, and there is a likelier necessity for operative intervention than in Group I.

The objects of radiological examination are two-fold :—

- (i) To determine whether the bony pelvis is large enough to permit descent of the head.
- (ii) To determine how the head may descend if the pelvis is large enough to receive it.

These are the quantitative and qualitative methods respectively. The proportionate sizes of the head and pelvis do not always give an accurate prognosis of the likely ease or difficulty of a labour. Even a major degree of disproportion may be overcome by the ability of the head to flex and mould with efficient uterine action. The smallest diameter is not necessarily an index of pelvic capacity because there may be useful compensatory variations in shape in other axes and planes.

Qualitative studies make quantitative analyses much more valuable and a knowledge of the pelvic shape and foetal-pelvic relationships gained by X-ray methods before and during labour will be advantageous to the obstetrician and will aid his judgment in the correct management of difficult labour and the treatment of arrest. Guidance and not dogma may be expected from radiological studies.

The writings of Caldwell and Moloy have been criticised mainly as to their classification of pelves which has been called cumbersome and unscientific (23). But the classification *per se* is not of fundamental importance; what is important is their realisation that shape and form means much more than the acceptance of such narrow terms as the "generally contracted pelvis."

At what period of gestation should X-ray investigation be undertaken? The radiologist's task becomes more difficult as pregnancy advances, and pelvimetry should preferably be performed in the early months. The study of disproportion and volumetric comparisons must obviously be made near full term. It is therefore suggested that full pelvimetry should be done early, but that foetal pelvic relationships be investigated at or near full-term, or during labour, by a limited examination in which stereoscopy is valuable.

What should guide the selection of cases for X-ray examination?

Some enthusiastic workers have advocated routine pelvic studies on all primiparous cases.

There is some justification for this attitude when it is remembered that even significant anatomical variations may be overlooked on competent clinical examination, especially in primigravidæ.

However, it must be remembered that each full study of the pelvis is time-consuming and costly. Thus in primigravidæ it would be reasonable to radiograph those cases in which clinical examination suggests some significant anatomical variation or when there is any doubt as to pelvic capacity. Obviously this will depend upon the adequacy and competence of the clinical examination. In multiparous women, whenever there has been a bad previous obstetric history with or without apparent cause, full X-ray study is justified.

X-ray examination will, at the very least, help to give a warning in potentially difficult cases, and will give encouraging confirmation in other cases in anticipated normal labour. In the borderline cases in which the obstetrician seeks most help, X-ray examination will often leave doubt as to the wisest course to pursue; but in this latter type of case, there is still much to be learned from radiological methods applied during labour in suitably equipped institutions.

The writer thus advocates a wider use of X-ray examination in clinically selected cases rather than an exclusion of X-ray methods or their routine and sometimes purposeless adoption. The examination should be made thoroughly; it is a great mistake to try and extract maximum information from radiographs of limited number or poor in quality taken with inadequate equipment.

### DEMONSTRATION OF THE PLACENTAL SITE AND PLACENTAL PRÆVIA

In obstetric practice it is sometimes desirable to ascertain the site of the placenta and this is often not determinable by clinical examination alone.

Radiographic examination may be distinctly helpful and methods have been devised to determine the placental site. Two methods—amniography and thorium placentography—are of academic interest but have little practical value and will be dealt with briefly. Two further methods—direct radiography and

cystography in suspected placenta prævia—are harmless, and their value is becoming more widely recognised.

**Amniography.** Amniography is performed by the injection of an opaque fluid substance directly into the amniotic fluid. The most suitable media are those used for intravenous urography (uroselectan B, for example). Early investigators in this field used strontium iodide (Munro Kerr and Mackay (24) ) but several foetal deaths occurred. Uroselectan is the safer medium but almost invariably the onset of labour follows amniography, and hence the method should only be used late in pregnancy, when the onset of labour may be reasonably welcomed. Burke (25) has shown that amniography will almost certainly indicate the placental site. The amniotic fluid is rendered relatively opaque and contrasts with the foetal soft tissues and the muscular uterine wall. The placenta will appear as a filling defect at the expense of the amniotic cavity. The risks of the method scarcely justify its use when harmless methods will often show the placental site.

**Thorium Placentography.** Erhardt (26) has shown that the placenta will “take-up” certain substances injected into the maternal blood stream. Such substances are thorium dioxide and tri-iodostearic acid, and in experimental animals the placenta has been clearly visualised owing to its radiopacity. Thorium is contra-indicated in the human subject because of its fixation in the reticulo-endothelial system and its radio-activity. The use of tri-iodostearic acid has not been tried out in clinical work, but may one day prove useful.

### Direct Radiography and Air Cystography

Snow (27) has made an especial study of the soft tissues in pregnancy and finds that a normally-placed placenta is frequently demonstrable as an opacity merging with the uterine wall and considerably increasing its apparent thickness. The shadow of the placenta is sometimes indented by the foetal limbs, but is separated from them by thin linear translucencies due to the foetal subcutaneous fat and the vernix caseosa. The placental shadow usually occupies about one-third of the uterine wall space as seen in lateral views. If the placenta is not seen at the fundus or distinctly in the main body of the uterus, it may well lie in the lower uterine segment.

In suspected placenta prævia, Snow (27) injects 150 c.c. of air into the bladder and studies the relationships of the bladder fundus to the foetal skull in vertex presentations. Brown and

Dippel (28) have been able to localise the placenta in 85 per cent. of 200 cases examined by the following simple technique: (i) a simple lateral view of the uterus is taken, the technical factors being designed to give a full contrast of the soft tissues; ordinary illumination is used for viewing the posterior parts of the films, but intense illumination is used for the anterior part. Hydramnios makes it impossible to visualise the placenta.

(ii) With air injected into the bladder, antero-posterior and lateral views are taken with a technique usually used for the lumbar spine. The relationships of the bladder fundus to the foetal parts is usually clear. These authors believe that air is a better contrast medium than the opaque sodium iodide.

### Cystography in the Diagnosis of Placenta Prævia

Ante-partum hæmorrhage is always a cause of concern to the obstetrician. Whilst clinical examination will often determine if a placenta prævia is present, there are certain cases in which the obstetrician will welcome help in diagnosis if this can be achieved by simple methods.

The investigations of Ude and Urner (29) on cystography in placenta prævia were first published in 1934 and they claimed that their method had considerable value. These claims have now withstood critical tests of other workers and their method may be advocated.

The object of the method is to analyse the soft tissue space seen between the fundus of the bladder and the foetal skull, the former containing some opaque substance. This space normally is occupied by the thickness of the lower uterine segment, the foetal scalp, the peritoneal reflection and the thickness of the bladder wall. The space in normal cases seldom exceeds 1.0 cm. in thickness. When this space is increased then it is very probable that the placenta is interposed between the foetal skull and the lower segment wall. The only other reported causes of an increase in the thickness of this space are blood clot and a presenting arm.

**Technique.** Although simple, technique must be precise. The rectum and pelvic colon are cleansed by a low enema; this is of great importance and failure to do this certainly accounts for some of the diagnostic errors reported. The bladder is then catheterised and 25-40 c.c. of a suitable contrast solution, *e.g.*, 10 per cent. sodium iodide, is instilled. It is a mistake to use too much contrast fluid. Antero-posterior and oblique views of the bladder

are taken, centering immediately above the symphysis pubis; occasionally a lateral view is of some value.

If a low-lying placenta is present, the space or gap will be appreciably increased, symmetrically with a central placenta prævia, asymmetrically with a partial placenta prævia. At first it was only considered that the method was applicable in vertex presentations, but Ude has found it also useful in breech presentations.

In the originator's first series (29), 35 cases of ante-partum bleeding were investigated: 14 showed positive radiological evidence of placenta prævia, and in 13 of these the diagnosis was confirmed. Twenty-one cases showed normal X-ray appearances, and in none of these did the later clinical course suggest placenta prævia. In their second series (30) there were 44 cases; the X-ray findings were negative in 39 cases and positive in 5 cases (4 central, 1 partial). Operative and parturition findings showed that there was only one error, one case regarded as having placenta prævia showing a normal placental site.

The writer has investigated a series of 20 cases showing ante-partum hæmorrhages; 15 showed no radiological sign of placenta prævia; 5 showed positive signs; there was one error, one case being reported as having placenta prævia for which there was no later confirmation.

It is, of course, necessary to stress that clinical and radiological findings must be carefully correlated, and when there is disagreement, full re-examination should be undertaken.

### THE URINARY TRACT IN PREGNANCY

In view of the discussion in Chapter IV on Pyelitis of Pregnancy, comments in this section will be virtually restricted to a description of the radiological appearances during excretion urography after intravenous injection.

**The Urinary Tract in Normal Pregnancy.** The advent of excretion urography has given us an excellent "physiological" method for studying the urinary tract, especially in pregnancy. The examination is innocuous to both mother and foetus. The "physiological" dilatation and adynamia of calyces, pelves and ureters may be closely studied and is of great interest in view of the common occurrence of pyelitis of pregnancy, which is said to occur in 6-8 per cent. of all pregnancies. The "physiological" dilatation was found by Luchs (31) to occur in 41 of 50 cases, by Schumacher (32) in 100 of 100 cases, by Seng (33) in 78 of 78 cases,

and by Kretschmer and Heany (34) in 43 of 44 cases. In the latter series, the second that these authors have published, two-thirds of the cases showed dilatation between the second and fifth months, and 90 per cent. between the sixth month and "full-term."

### The Causes of Physiological Dilatation and Adynamia

At least three factors probably play some part :—

(i) Pressure obstruction from the enlarging uterus. This is certainly not the sole factor ; a few women go through to "full term" without demonstrable urinary tract dilatation, and cases have been reported in which there was considerable dilatation in early pregnancy which lessened as gestation advanced.

The effect of uterine pressure on the ureters is dependent to some extent upon the angle of the pelvic inlet and the type of pelvis ; the usual supine posture used in routine radiography of the urinary tract will emphasise this pressure effect.

(ii) Hypertrophy of the lower ureter in pregnancy would account for some obstructive dilatation but not, *per se*, for the adynamia.

(iii) Hormonic influence. This is discussed in Chapter IV.

### Radiographic Appearances in Normal Pregnancy

Excretion urography is a very satisfactory examination in pregnancy because the stasis and compression of the ureters by the uterus will produce pyelograms almost as clearly defined as those obtained on retrograde pyelography.

Preliminary films of the urinary tract should always be taken. The rate of renal excretion is unimpaired and in the 10–40 minute period following injection an increasingly clear delineation is obtained of the pelves, calyces and ureters down to the pelvic brim. There is an appreciable delay of urinary clearance and well-defined pyelograms are often seen three hours after injection. The dilatation is such that the general form of the pelvis is retained and the poverty of pelvi-ureteric sphincter action leads to an appearance of a continuous fluid pelvi-ureteric column. The cupping of the minor calyces is lost, and the outward concave calyx margins are straightened but seldom, in the absence of infection, become frankly convex outwards.

Thus in normal pregnancy, the outstanding features are :—

(i) Normal excretion rate from the kidney, (ii) slow pelvi-ureteric clearance of the urine, (iii) moderate dilatation with a pelvi-ureteric column effect.

Physiological dilatation may be unilateral, which is an important fact to consider when urinary infection is present.

### Radiological Appearances in Pyelitis of Pregnancy

Mild forms of pyelitis may show little or no change above that which is attributable to the physiological alterations in pregnancy. Moderate and severer infections show the following changes :—

(i) A varying depression of excretory function of the kidneys, sometimes profound, *i.e.*, a delay in the appearance of the opaque medium and a poor delineation of the pelvi-calycine anatomy.

(ii) Extreme dilatation, especially of the minor calyces : the appearances are those of a severe infected hydronephrosis of long-standing without pregnancy.

The dilatation and functional depression may increase rapidly in severity and also tend to recover rapidly after delivery. If puerperal recovery is not rapid, the patient should be submitted to a full urological investigation. Pyelitis in pregnancy may be complicating a pre-existing but unsuspected inflammatory or obstructive lesion. The lower ureter may become involved in a pelvic cellulitis secondary to cervical laceration. Again, cases have been reported in which, during pregnancy, a stricturous lesion developed in the ureter at the level of the pelvic brim. The treatment of such cases can only be adequate if an accurate diagnosis of the causative factor is made ; excretion urography is probably the most helpful approach in such cases.

Urography is undoubtedly of great value in the investigation of the urinary tract in pregnancy. It is an essential guide in therapeutic control. If urographic methods were more commonly used, the disastrous necessity of post-partum nephrectomy would seldom arise.

I should like to express my thanks to Dr. Courtney Gage for his permission to include some of his illustrations from the 4th Edition in the present work.

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## APPENDIX

### Dr. Courtney Gage's Method of Charting the Shape and Size of the Pelvis

(Original description by Dr. Gage from earlier editions of this book)  
(See Fig. 12)

"A more exact method, and one that gives the actual shape of the pelvis as well as all the diameters, is based on the same sitting position. It has been used by the writer for the last fourteen years with uniformly good results. The top of the symphysis and

the top of the spinous process of the fifth lumbar vertebra indicate the plane of the pelvic inlet. The patient is adjusted so that these two landmarks are equidistant from the film.

"The distance from the anti-cathode of the tube to the film should be measured, also the distance from the top of the symphysis to the film.

"The tube is centered over the estimated centre of the pelvic inlet: this will be well above the umbilicus or over the top of the uterus if the abdomen is lax or protruberant at term. The centering should be done as carefully as possible but it does not matter if it is not very exact if the full technique here described is to be carried out. An aluminium filter, 1 or 2 mm. thick, should be used beneath the tube; this should be a routine filtration for all abdominal radiography. From the centre of this, and in the line of the normal ray, a small metallic plumb bob should hang and remain in position while the radiograph is being taken; in this manner, the point of incidence of the normal ray on the film will be recorded.

"The measurements should be recorded on the film before development, where they will form a permanent record for reference at any future time.

"If there is any difficulty in determining the position of the spinous process on account of gross deformity or obesity, a preliminary lateral film may be taken with a metal marker on the skin over the spinous process; from this film the exact position can be determined. When the film is dry, make a bold tracing of the pelvic outline from the tube side of the film, clearly indicating right and left; and place a dot in the centre of the shadow of the plumb bob. Armed with the tracing and a length of round elastic, to one end of which a plumb bob is attached, place the tracing on the X-ray table and pin it there with a small drawing pin through the centre of the dot, tie the elastic on the metal tip at the end of the X-ray tube and adjust the tube to the same height as when the radiograph was taken so that the plumb bob just clears the table, and move the tube until the tip of the plumb bob overhangs the dot on the tracing.

"The elastic is now in line with the normal ray, the ray that produced the shadow on the film, and conditions are now identical with those under which the radiograph was taken. One small accessory is necessary, a heavy small metal base to one corner of which a small vertical metal rod is attached marked with an appropriate scale in fractions of an inch or centimetres. The

scale should be clear and well defined. Next tie a loop knot in the elastic so as to shorten it by some inches; now take the elastic in the left hand, bending it over the thumb or finger nail, stretch it tight and place the thumb nail on the outline of the pelvis, approach the vertical scale so that it touches the stretched elastic at the height of the plane of the pelvic inlet from the film, and at the foot of the scale place a dot; the tracing can now be rotated until the complete circumference of the pelvis has been made in dots at suitable intervals. The dotted outline shows the exact shape and dimensions of the pelvis; the whole operation takes less than five minutes. Often methods are perhaps simpler but if the pelvis is deformed a chart showing the exact shape, fully corrected in size, gives a better appreciation of the obstetric possibilities than simpler measurements of the diameters, which may be misleading. The chart may show at a glance that the presentation is a favourable one for that particular deformity of the pelvis or otherwise."

## PART II. GYNÆCOLOGY

### CHAPTER VIII

#### CANCER OF THE UTERUS

##### SECTION I—CANCER OF THE CERVIX

MEDICAL opinion the world over appears to be more or less agreed that the Westheim operation or other form of surgical attack on carcinoma of the cervix has been superseded by radium therapy with the usual addition of deep X-rays. During war-time the difficulties attendant upon the use of radium have occasionally resulted in the selection of surgical treatment for these cases in certain localities; but the generalisation with which this chapter starts may still be accepted.

The drift of opinion against surgery and in favour of some form of radio-therapy is clearly the outcome of consideration of the results obtained by the methods in question. And yet when one looks into this matter carefully it must be admitted that there is still room for doubt before any unanimous decision can be reached. It would appear certain that the five-year results obtainable by radium and X-rays are definitely better than are those claimed for surgery. It is far less certain that the ten-year results will bear anything like such favourable comparison.

Again, there is the tendency, which one senses over and over again in the reports, for radium therapy centres to present their results, not with a strictly judicial fairness, but in a way which tends to show *radium therapy in a more favourable light than it really merits*. There is, for instance, a patent selection of cases in one famous continental centre. When such bias is encountered the suspicion is instantly raised that statistical dodges or other subterfuges have been employed to paint the results of therapy in too rosy colours. But even if allowance is made for this possible tendency, it will be seen that at least the five-year radium figures are highly impressive.

##### The Results obtained by Radiotherapy

Anybody who has been to Stockholm and seen the work of the Radium-hemmet cannot fail to be impressed by the fact that all cases of carcinoma of the cervix occurring in north and middle Sweden are there dealt with. No matter how advanced the disease

may be, the case must be accepted and must appear in the records. Furthermore, the treatment employed for all the cases is uniform; cases are followed up with meticulous care and the results are recorded with precision. The results obtained at the Radiumhemmet by radium, and latterly by radium combined with deep X-ray therapy, have shown a consistently level standard of success. These figures may therefore be regarded as a fair sample of the percentage of cures likely to be obtained by this therapy in the hands of skilled technicians.

It is obvious that there will be minor differences between these and the results obtained at other clinics. But the reports from some clinics are so very optimistic that there can hardly fail to be some suspicion that the comparison with the Stockholm figures is not absolutely exact. If one tries to visualise the methods by which errors could creep in, either by accident or design, it will at once be seen that should there be any selection of cases, or should there be any method of excluding the advanced cases, either with or without the knowledge of the honorary staff, then the percentage of "cures" will automatically be much greater than would appear in a truly representative analysis.

Again, if the tendency of the staff is to call only quite early cases Stage II. and cases slightly more advanced, yet still early, Stage III., then the results obtained in such cases will obviously seem better than will be those achieved by anybody who adheres with greater strictness to the League of Nations system of grouping.

This classification of cases into four stages is generally accepted in Europe, though the Schmitz classification into five classes is often used in America.

The League of Nations new (1937) Classification of the four clinical stages of uterine cancer is as follows:—

Stage I. The carcinoma is strictly confined to the cervix.

Stage II. The carcinoma infiltrates the parametrium on one or both sides but has not invaded the pelvic wall—Stage II., parametrium.

The carcinoma infiltrates the vagina but does not involve its lower third—Stage II., vagina.

Endocervical carcinoma which has spread to the corpus—Stage II., corpus.

Stage III. The carcinomatous infiltration of the parametrium has invaded the pelvic walls on one or both sides. On rectal examination no cancer free space is found between the tumour and the pelvic wall—Stage III., parametrium.

The carcinoma involves the lower third of the vagina—Stage III. vagina.

Isolated carcinomatous masses are palpable on the pelvic wall (irrespective of the extent of the primary cervical growth)—Stage III., isolated pelvic metastases.

Stage IV. The carcinoma involves the bladder as determined by cystoscopic examination or by the presence of a vesico-vaginal fistula—Stage IV., bladder.

The carcinoma involves the rectum—Stage IV., rectum.

The carcinoma has spread outside the true pelvis (*i.e.*, below the vaginal inlet, above the pelvic brim, distant metastases)—Stage IV., distant spread.

General rules to be observed: When allocating a case to a stage, nothing but the facts revealed by examination should be taken into account, and this classification should remain unchanged. The fact that a single case presents two or more of the features which characterise a particular stage does not affect its staging. In endeavouring to discriminate between an advanced example of a particular stage and an early example of a succeeding stage, *it should be a general rule to allot cases to the prognostically more favourable earlier stage*, so as not to raise unduly the proportion of favourable results in the less advanced grades.

Assessment of the value of radium treatment is rendered difficult by failure to grade cases strictly in accordance with the above classification, by any tendency to select cases, by the differences in technique that naturally obtain at different clinics and by many other factors. It is at least to be hoped that those responsible for the issue of statistical tables, when giving their results, will realise that although bad results may condemn any method of treatment, results that are too good to be accepted without some suspicion are almost equally destructive; and that anybody responsible for publishing results which in any way do not completely represent the exact truth of the matter is in all probability doing harm to the cause which he really wishes to advocate.

Furthermore, the average reader will be able to get a clearer idea of the value of any given treatment at any given clinic when such clinic together with all others adopts some standard scheme of publication. What the average man wants to know is this: out of 100 cases seen how many are alive and free from cancer at the end of five, ten, or more years. That is to say, the "absolute" cure rate among all cases seen with no allowance

made for cases not treated, those that have died of intercurrent disease, etc.

Many of our difficulties in appreciating the position and in presenting the facts is due to the failure of reporting centres to conform to such a scheme. So if we are now to attempt to compare the results by different workers, it will be convenient first to quote the figures from Stockholm (1). These form a reliable basis for comparison.

*Table of Results Obtained (Radium-hemmet)*

Year of treatment	No of cases treated	Percentage of five-year cures
1920	96	27.1
1921	115	23.5
1922	130	20.0
1923	105	23.8
1924	149	23.5
1925	134	14.2
1926	143	25.9
1927	143	25.0
1928	128	23.4
1929	152	30.3
1930	198	25.2

The very low figure for 1925 is explained partly by the large number of advanced cases encountered that year (31.4% were in Stage IV., as compared with their average Stage IV. figure of about 23%).

If the results are not taken for individual years but are grouped in periods, we still see remarkable consistency in the results, but with some slight tendency to improvement.

*Case Results during the Different Periods*

	No of cases treated.	No of five-year cures	Percentage of five-year cures.
1914-1919 .	296	65	22.0
1920-1925 .	730	159	21.8
1926-1929 .	566	154	27.2

The reason for the improvement is possibly that the cases are coming for treatment at an earlier stage of the disease as is evidenced by the following table:—

*Table showing Improvement of the Material*

	Total No. treated.	Stages I. and II. percentage.	Stages III. and IV. percentage.
1914-1919 .	296	22.3	77.7
1920-1928 .	1,143	41.8	58.2

For comparison with these results, figures must be taken more or less at random from the literature; space does not permit of the publication of more than a small fraction of the total bulk available. And when seeking comparison it is well to remember Heyman's (2) words: "The more one studies these questions (the possibility of comparing the results from different clinics, etc.), the more pessimistic one becomes in regard to the possibility of forming an opinion as to the value of the different methods of treatment by means of a comparison of published results."

### COMPARISON OF STATISTICS

So far we have merely considered the Stockholm figures with the idea of using them as a basis for comparison with other statistics. How do they compare with the bulked figures from other countries?

The aggregate figures from 16 centres from all over the world, as reported in the Summary of the Annual Report on the Results of Radiotherapy (3) are as follows:—

	Per cent. of cases treated
Cases seen with a view to treatment .	9,051
Cases treated . . . . .	7,958 = 87.8%
Alive without recurrence, five years (includes 31 cases without micro- scopical verification) . . . . .	2,194 = 27.6%
Alive with recurrence, five years . . . . .	128 = 1.6%
Died of cancer . . . . .	5,368 = 67.5%
Died of intercurrent disease . . . . .	163 = 2.0%
Lost . . . . .	105 = 1.3%

The percentage of five-year "cures" among the cases . . .  
(i.e., 9,051) works out at 24.2.



The cases treated were allocated to stages as shown in the next table.

Stage.	No	Per cent.
I. . . .	871	10.9
II. . . .	2,305	29.0
III. . . .	3,420	43.0
IV. . . .	1,860	17.1
Unclassified . . .	2	—
	7,958	100.0

N.B.—87.8% of cases seen were treated.

The results according to stages can be tabulated thus :—

Stage.	No treated	Alive five years, no recurrence.	Relative cure rate.
I. . . .	871	498	57.2
II. . . .	2,305	867	37.6
III. . . .	3,420	754	22.0
IV. . . .	1,860	75	5.5
Total . . .	7,956	2,194	27.6

It must also be noted that among the 16 centres which report in this League of Nations "Annual Report," nine publish an "absolute cure rate." Five of these show a rate of 30% or better—very gratifying results.

It will be seen that bulked figures suggest that somewhere in the region of 25% is the figure representing the five-year-cure rate obtainable by radium therapy. This is in rough agreement with the Stockholm figure.

Before proceeding to the more detailed study of the statistics published by various individual centres it will be instructive to see if figures throw any light on the question of which radiological technique yields the best results. According to Todd (4) the following table shows the results achieved by the different

techniques. It is difficult to draw any definite conclusion from these figures since, as will appear later, it would seem that a considerable number of cases presenting themselves for treatment by the Paris method are not accepted. But the figures as they stand seem to indicate a greater chance of success if the Paris technique is followed. It must again be emphasised that this remark must be accepted with reserve.

*Comparison between Results obtained by the Three Chief Techniques of Treatment of Carcinoma of the Cervic Uteri*

Technique.	No. of cases treated.	Five-year survivals.	Percentage.
American .	3,130	654	20.9
Stockholm .	1,203	281	23.4
Paris .	1,106	305	27.7

**STATISTICS FROM INDIVIDUAL CLINICS**

We now begin the direct comparison between the results obtained by definitely specified methods and those obtained at Stockholm.

The best results in this country have been obtained by the Stockholm method of treatment at the Marie Curie Hospital. The published results of their cases extracted from the League of Nations Annual Report, 3rd Volume, show that a total of 588 were treated between 1925 and 1931 and the figures from this hospital are so remarkably good that they must receive considerable space here. The following table will show many of the facts in a concise form. It must be realised that these results are among the case *treated*, i.e., the figure in the last column is the "relative" cure rate.

*Results obtained in 588 Cases at the Marie Curie Hospital, 1925 to 1931*

Stage.	No. of cases treated in each stage.	Alive, no recurrences for five years.	Relative cure rate per cent.
I.	29	24	82.8
II.	105	67	63.8
III.	350	109	31.1
IV.	104	9	8.7
Total	588	209	35.5

A different way of expressing the same figures which brings out the comparatively small number of cases in Stages I. and II. and which shows the salvage out of every 100 cases treated is shown in the next table.

Stages.	Percentage of cases treated in each stage	Salvage per 100 cases treated.
I. . .	4.93	4.0
II. . .	17.8	11.4
III. . .	59.5	18.5
IV. . .	17.6	1.6
Total (approx.)	100.0	35.5

Further study of the above two tables reveals that in Stages I. and II. there were only 194 cases treated or 22.75%. The salvage (five-year cures) among these amounted to 91 cases, or 67.8% of cases in the first two groups. This sounds an amazing figure. But it does not sound quite so remarkable if expressed as a salvage of 15.6 out of every 100 cases treated—treated be it again noted. For the results at this hospital are shown as "relative" cures, i.e., cures among the cases treated and not among the total number seen.

In a similar analysis Stages III. and IV. will be observed to have included 454 cases or 77.25% of the total treated. The five-year cures among these totalled 118 or 26% of the cases treated in these stages. Expressed as a salvage per 100 cases treated the figure is 20. The total salvage per 100 cases treated is the sum of this 20, plus the 15.6 mentioned in the last paragraph, and, of course, agrees with the "relative" cure rate.

If Stages I., II. and III. are grouped together the figures are still remarkable, viz., 484 cases out of 588 or 82.3%. Among these the five-year cures were 200 in all or 41.3% relative cure rate.

It becomes evident that this hospital must achieve some astonishing results in the treatment of Stage III. cases and the detailed table which follows seems worthy of reproduction in support of this argument. All the cases shown in this are Stage III.

and the figures indicate the cases treated in this stage during each of several years, and the numbers alive and without recurrence at the end of 5, 6, 7, 8, 9 and 10 years respectively.

Year.	No. of patients treated in Stage III.	Alive without recurrence after period of observation of years.						Relative cure after period of observation of years					
		5	6	7	8	9	10	5	6	7	8	9	10
1925-6	50	14	11	11	10	10	9	28.0	22.0	22.0	20.0	20.0	18.0
1927	28	9	9	9	8	8	6	32.1	32.1	32.1	28.6	28.6	21.4
1928	46	16	15	15	13	12	—	34.8	32.6	32.6	28.3	26.1	—
1929	70	20	18	16	13	—	—	28.6	25.7	22.9	18.6	—	—
1929	70	20	18	16	13	—	—	28.6	25.7	22.9	18.6	—	—
1930	81	27	24	22	—	—	—	33.3	29.6	27.2	—	—	—
1931	75	23	22	—	—	—	—	30.7	29.3	—	—	—	—
Total.	350	109						31.1					

Two other important centres of radio therapy are The Radium Institute, London, and the Mount Vernon Hospital. These two are now amalgamated but their joint results are not yet available. The most recent results of the cases at the Mount Vernon Hospital have been supplied by Mr. Donaldson in a private communication. The following table gives a concise picture of the results, 5, 6, 7, 8, 9 and 10 years after treatment.

#### *Mount Vernon Hospital and Radium Institute*

Year of Treatment.	No. of cases classified.	Not traced.	Radiated.	No. alive in Stages I. and II	Percentage alive in Stages I. and II	No. alive all stages.	Relative cure or percentage alive all stages.	No. of years after treatment
1930	43	0	42	6	35	8	19	10
1931	53	1	53	7	41	14	26.4	9
1932	55	1	55	7	46	15	27.2	8
1933	39	0	39	1	14	6	15.4	7
1934	46	0	45	7	50	12	26.6	6
1935	59	2	59	7	30	11	18.6	5

If all the cases treated five to ten years ago be aggregated we find that 295 were classified. Of these 66, or 22.5%, are alive five or more years later. Again, of the 295 cases classified, 93, or 31%, were placed in Stages I. and II. Of these early cases 35, or 37.6%, are alive five to ten years later.

## Some American Figures

The figures for the Women's Hospital, New York, for the year 1932 as reported by Dr. George Ward are as follows. The cures are those alive and well five years later, *i.e.*, 1937.

## WOMEN'S HOSPITAL, NEW YORK

*Cases treated during Year 1932*

Total number examined with a view to treatment . . . . .	42
Total number radiologically treated (and microscopically verified) . . . . .	41
Alive without recurrence at end of five years,	
Stages I. to IV. . . . .	19
Absolute cure rate . . . . .	45.2%

Contrast this very high figure for the absolute cure rate with the figure from the Memorial Hospital, also of New York (*vide infra*) where the absolute cure rate is nearer to that which usually obtains, and at once some explanation seems necessary. This may lie in the material which is dealt with at the Women's Hospital. For their figures reveal that Stages I. and II. comprise 37 of the 41 cases treated with 18 cures. In other words, a relative five-year rate of nearly 49% in those two Stages. Such a figure is reasonable.

The supposition that the material attending this hospital is rather unusual, is supported by the fact that in Table 7, p. 40, of the League of Nations Annual Report (3rd Volume), very few cases appear in the Stage IV. column. It also appears there that, although the percentage of cases in Stages I. and II. had not always been as high as in 1932, the cases dealt with at this hospital do tend to be staged as very early ones, at any rate, in the more recent years.

Perhaps the hospital figures over a longer period represent a fairer average. For the remaining figures concerning the results at the Women's Hospital we are indebted to a personal communication from Dr. Sackett. His figures are extremely valuable, especially as they include five-year and ten-year absolute survival rates representing the results in a moderately large number of cases. But it should be noted that the Schmitz and not the League of Nations' classification is employed.

Table showing Five-year Results : Women's Hospital, New York

Schmitz class.	All classes.	I.	II.	III.	IV.	V.	I. and II., early.	III., IV. and V., late.
Total seen . . . . .	711	22	126	500	58	5	148	563
Irradiated . . . . .	679	22	125	497	30	5	147	532
Living five years . . . . .	196	14	68	114	0	0	82	114
Absolute five-year survival per cent. . . . .	27.6	63.6	53.9	22.8	0	0	55.4	20.2
Relative five-year survival per cent. . . . .	28.9	63.6	54.4	23.7	0	0	55.8	2.4

Cases seen February, 1919, to December 31st, 1935. Fourteen (or 2.1%) were untraced and counted dead of cancer.

Table showing Ten-year Results : Women's Hospital, New York

Schmitz class.	All classes.	I.	II.	III.	IV.	V.	I and II., early.	III., IV. and V., late.
Total seen. . . . .	534	10	94	379	45	6	101	430
Irradiated . . . . .	512	10	94	378	26	4	104	408
Living ten years . . . . .	101	6	42	53	0	0	48	53
Absolute ten-year survival per cent. . . . .	18.9	60.0	44.7	14.0	0	0	46.2	12.3
Relative ten-year survival per cent. . . . .	19.7	60.0	44.7	14.0	0	0	46.2	13.0

The cases were seen between February, 1919, and December 31st, 1930. Eighteen (or 3.5%) were untraced and counted dead of cancer. We will now take the 1932 results from another New York Hospital.

### THE MEMORIAL HOSPITAL, NEW YORK

Reported by Dr. W. P. Healy

#### Cases treated in 1932

Total number examined with a view to treatment . . . . .	159
Total number radiologically treated (2 not microscopically verified) . . . . .	141
Alive without recurrence at end of five years . . . . .	40
Absolute cure rate . . . . .	25.2%
Relative cure rate . . . . .	28.4%

## Some Continental Figures

*Institut du Radium, Paris*

Reported by Dr. A. Lacassagne

*Cases treated in 1932*

Total number examined with a view to treatment . . . . .	181
Total number radiologically treated (all microscopically verified) . . . . .	101
Not treated . . . . .	80
Alive without recurrence at end of five years	52
Relative cure rate . . . . .	51.5%

(The absolute cure rate would work out at the greatly reduced figure of 28.7%)

*Table showing the Stages of the Cases treated in Paris*

Stage	No. of cases treated	Percentage of those treated
I. . . . .	18	17.8
II. . . . .	43	42.6
III. . . . .	34	33.7
IV. . . . .	6	5.9
Total . . . . .	101	100

Analysing these figures we see that at this hospital 61 cases or 60% were in Stages I. and II. This is presumably explained to a large extent by the 80 cases which were not radiologically treated.

The results are therefore vitiated by the large number of cases which was not accepted for radiological treatment. It is only fair therefore to express these results in a different manner. Thus, of 181 cases seen, 61 were in Stages I. and II. Of these 37 were alive without recurrence at the end of five years—a salvage of 20.44 per 100 cases seen. Similarly, of the 40 cases treated, although they belonged to Stages III. and IV., 15 were five-year cures—a further salvage of 8.3 per 100 cases seen. The total salvage (or “absolute cure rate”) is thus 28.7%, which contrasts with the “relative cure rate” of 51.5 per cent

*Brussels*

Reported by Professor J. Murdoch

*1932 Results*

Total number examined with a view to treatment . . . . .	93
Total number radiologically treated (3 not verified microscopically) . . . . .	83
Alive without recurrence at end of five years	21
Absolute cure rate . . . . .	22.6%
Relative cure rate . . . . .	25.3%

*Aggregate Results of Previous Years*

Total number examined with a view to treatment . . . . .	457
Total number radiologically treated . . . . .	398
Alive without recurrence at end of five years . . . . .	96
Absolute cure rate—five years . . . . .	21.0%

*Ten-Year Results*

Total number examined with a view to treatment . . . . .	73
Total number radiologically treated . . . . .	60
Alive without recurrence at end of ten years . . . . .	10
Absolute cure rate—ten years . . . . .	13.3%

*Munich, 1924-1925*

Stage.	No.	Five-year survivals.	Percentage.
I. . . . .	99	49	49.4
II. . . . .	91	21	23.1
III. . . . .	129	23	17.9
IV. . . . .	85	4	4.9

Percentage five-year cure of all cases, 24

*The Value of Supplementary X-ray Therapy*

It appears gradually to be becoming the belief that improved results are being obtained by supplementing radium treatment by deep X-ray or by tele-radium. But Heyman (14) is not by any means convinced. He says "I would not dare stress as a fact, as is generally done in the literature, the advantage of combined radium and Röntgen treatment over brachy-radium treatment alone."



The outstandingly good results claimed by the Marie Curie Hospital would seem to suggest that supplementary X-radiation is not necessary. For, apart from a few cases, they only started to use deep X-rays in 1934. And their figures quoted earlier in this chapter were for cases treated in 1932 and before. Nevertheless they have been using supplemental X-ray on an increasing scale since 1934, at any rate, for as many Stage II., III. and IV. cases as possible.

On the other hand, Paris claims that their superior results are due to the use of external radiation supplementary to internal radium therapy. They say that there has been no important alteration in their internal radium technique since 1922. Since 1923 an increasing number get additional X-rays. And now, practically all except Stage I. cases receive it. Lacassagne (5) goes even further and suggests that still better results in Stage I cases would be attainable were supplementary X-rays employed.

But are the Paris results superior? Their published five-year cures for 1932 cases were the highest in the world, 51.5% as compared with 37.2% at the Marie Curie Hospital, which came second. We have already indicated that a considerable amount of the apparent success at Paris can be discounted owing to the large number of cases that were not accepted for treatment.

But when Paris contrasts its own figures for a given period of time with its own figures for another period, the same criticism cannot be brought forward. Lacassagne's published figures contrasting results before and after the addition of deep X-ray therapy are quoted by Swanberg (6) and it is just that they should be accepted. But there is only a short period of time covered by the combined treatment.

*Figures showing Benefit of Supplemental X-ray.  
(After Lacassagne.)*

Period.	No of patients treated	Relative five-year cures		
	Stages II, III and IV	Stage II	Stage III	Stage IV.
1923-32 internal radium alone	153	38%	6%	0%
1932 combined internal and external irradiation . . .	83	39.5%	41.2%	16.7%

Admittedly there is only a short period of time covered by the combined treatment but these figures point strongly to the conclusion that deep X-ray should be used as a supplement to radium therapy. And indeed such appears to be the accepted opinion as more and more clinics are using the combined treatment. Further consideration of the theoretical desirability for such supplement and of the technique to be employed is given in the chapter devoted to X-ray therapy later in the book.

### GLAND INVOLVEMENT

The incidence and effect of glandular involvement is important. Most observers agree that in cases of carcinoma of the cervix, glandular metastasis is present in about one-third.

Leitch found that in over 900 post-mortem examinations of women dying of cancer of the cervix not operated upon, only 35% had metastasis in the regional glands. Glandular growths are chiefly found either in young patients or in patients with advanced growths, and when they occur they definitely influence prognosis for the worse, even if the pelvic cellular tissue is completely removed by surgical treatment. It is quite impossible to form any kind of clinical diagnosis of glandular involvement by mere abdominal, vaginal and rectal examination. It is not even feasible by palpation at operation for small soft glands may contain a malignant nucleus, while large hard glands on the other hand may show nothing but inflammatory reaction.

The influence of glandular affection on the prognosis is shown by Bonney (8), who divides his 500 cases of Wertheim's operation into 300, which had not gland involvement and 200 which showed this complication. Of the gland-free cases over one-half were alive and well five years after the operation. Among the 200 with gland involvement only 42, or approximately one-fifth, were equally fortunate.

Of Bonney's 415 cases operated on ten or more years ago 244 were gland free. Of these 103, or 42% were alive and well ten years later. Contrast this with what obtains in the 171 cases in which glandular involvement was found at the time of the operation. Among these cases only 28, or 16%, were alive and well ten years after the operation.

It will thus be seen that a patient having malignant regional glands has considerably less than half the chance of survival that has one who is free from glandular extension.

## DISCUSSION

One might perhaps sum up the position thus: By radium therapy in good hands 50% five-year cure of the cases in Stages I. and II. may be anticipated. Some clinics do better than this and some do worse, but about 50% is a fair average. Among the cases in Stages III. and IV. a five-year cure rate of 20% or even 30% has been obtained, but 10% would be accepted by most people as all that could generally be hoped for.

Then, if all the cases are considered together, a five-year cure rate of approximately 25% seems reasonably attainable. And this rate of success is achieved at the cost of an initial mortality rate, due to the radium, of about 2%.

The time has now come to compare these figures with those obtained as the result of operative treatment. In this country one of the first articles to contrast the results of radium treatment with that of operation in comparable series of cases was published by Fletcher Shaw and Dougal (7). Of 94 cases treated by radium before January 1st, 1931, they had 41.4% alive and well at the end of the five years. These included cases in all four of the stages of the disease. In contrast, the series of cases operated on by them showed 38.3% alive and well at the end of five years; and this percentage of success is among the earlier cases of the disease, *i.e.*, those operated upon.

The above figures for the results of operation are strikingly similar to those of Victor Bonney (8), who has recently reported that his five-hundredth Wertheim operation was done in April, 1936. He is therefore able to publish his five-year results among that number of cases and his ten-year results among 415 cases. These results are shown in the following two tables.

*Five-year Results : all Cases Operated on*

Well five years after operation . . . . .	201 = 40%
Recurrence before five years . . . . .	193
Lost sight of . . . . .	14
Died of other disease . . . . .	22
Died of operation . . . . .	70 = 14%
	<hr/>
	500
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*Ten-year Results : all Cases Operated on*

Well ten years after operation . . .	131 = 31 %
Recurrence before ten years . . .	178
Lost sight of . . . . .	28
Died of other disease . . . . .	21
Died of operation . . . . .	57
	<hr/>
	415
	<hr/>

If the cases "lost sight of" or "died of other disease" be excluded his ten-year cure rate among cases operated on would work out at 36%.

Now Bonney reckons his operability rate is 63%. It will be seen below that other surgeons also claim high figures. But most of us do not find that over half the cases of carcinoma of the cervix we see could be operated on. However, Bonney maintains that many seemingly advanced cases have removable growths and he insists, quite rightly in our opinion, that it is fallacious to call the radiotherapist's Stage I and II. cases comparable to the surgeon's "operable" ones. He says that many Stage III. cases are operable, and more, he has operated on them.

Anyhow, Bonney says 63% is his figure and from that figure he calculates his "absolute" results. In other words, his "absolute" results are as if his 500 cases operated on were among 800 cases seen. Not many would pass this! But accepting this basis of calculation his "absolute" five-year cure rate is 25% and his "absolute" ten-year rate 20%.

Some salvage may be expected from radiotherapy to the 37% among the cases he sees and finds inoperable. So by operation for the operable and radium therapy for the inoperable it is possible that a five-year absolute cure rate of possibly 30%, and a ten-year "absolute" cure rate of perhaps 24% may be attainable.

Bonney has another important remark to make in the article quoted and that is, that recurrence after Wertheim's operation "is practically incurable by any means at present known to us, and except as a placebo it is a wastage of effort and apparatus to treat it by radium."

The close similarity (nearly 40% five-year cures of the cases operated on) of the results of Wertheim's operation by three

*Some Results of Wertheim's Operation by Continental Surgeons*

Operator	Percentage of operability	Percentage of operative mortality	Percentage of five-year cures.
Wertheim .	50	13.8	39.26
Doderlein .	60	20.0	32.5
Franz .	81	14.1	40.5
Brumm .	61	12.6	50.3
Stoeckel .	—	19.4	43.0

surgeons in this country may thus be taken as a fair sample of what is achieved by this operation. If we now look at the figures from European countries (for some of these figures and for those concerning the Schauta operation we are indebted to Dr. Paul Salacz of Budapest), we find that the variations are not of great significance and, generally speaking, Bonney's summing-up of his results shows what results can be expected from surgery alone.

It might be argued that results such as these cannot be approached by the average gynaecologist who sees a relatively small number of cases of carcinoma of the cervix each year, and who will never have the opportunity of acquiring the experience and dexterity of such masters. His results therefore will not be so good as those shown above. But the same thing applies to radium treatment. It is a most unfortunate thing that every gynaecologist seems to think himself capable of giving radium therapy more or less by the light of nature. Only a comparatively small percentage have studied at Stockholm or Paris the details of the methods employed at these great centres. It is therefore a very welcome fact that, at least in this country, radium therapy is slowly becoming more and more the province of the relatively few who are really skilled in its use. But radium is still used in the treatment of carcinoma of the cervix by all sorts of people, expert and otherwise, and this perhaps explains why good results are achieved at some hospitals, while others cannot show anything like such figures.

While considering the results of surgical treatment, the operation of vaginal hysterectomy by Schauta's or similar method must be considered, though it is very rarely performed in this country. The immediate operative mortality of this operation is relatively small, Peham and Amreich (9) having only 6.27 per-

centage mortality in 907 cases. Their percentage five-year survivals number 37.7%.

Other figures are :—

Operator.	Percentage operative mortality.	Percentage five-year survivals.
Schauta . . .	6.6	34.5
Schuchart . . .	—	36.0
Kamniker . . .	6.3	48.3

The percentage of five-year cures by this method of treatment thus bears comparison with those achieved by the Wertheim technique. In fact, collected statistics (Pankow) show a slightly higher percentage cure by the vaginal operation than by the abdominal—38.2 as against 35.8. Its lesser mortality is at least unquestioned. Anselmino and Ocheke (10) state that several recent statistics of radical vaginal (Schauta) operations have a lower primary mortality than has that of irradiation treatment.

Perhaps one of the most didactic contributions to the discussion on the relative value of the Wertheim and the Schauta operation is a paper by R. Schroder (11). Of 604 cases seen, the cases operated upon totalled 50%. Wertheim's operation was generally done in the first half of the period under review and Schauta's in the second. The primary mortality in 178 Wertheim cases was 18% against 1.5% in the 124 Schauta cases. Moreover, the Schauta cases had a higher percentage of "lasting" cures—51% as compared with 36%.

If we now return to the consideration of the results achieved by radium, there are two points which must not be forgotten. Firstly, the initial mortality of radium therapy is not *nil* as is often stated, but figures from various clinics often show something between 2% and 4%. The lesser of these figures is probably the general average. Secondly, it is not always made clear in the literature whether or not deep X-ray therapy has been applied in addition to the radium, or, if it is applied, for how many years is often unstated.

The question is this. Is radium treatment preferable to operation? While bearing in mind the difficulty of obtaining a true comparison from statistical tables, it seems hardly possible to avoid coming to the conclusion that, generally speaking,

radium can do everything that surgery can in the attempt to cure cancer of the cervix—and can do it with a much lower initial mortality rate. Therefore, if we accept without question the figures for the results obtained by radium treatment, the Wertheim operation should be done only under exceptional circumstances. It will be brought forward in objection to this statement that the Wertheim's operation will save certain cases with early gland involvement that would not have been permanently benefited by radium. Possibly true; but the figures of the end results must be allowed to speak for themselves. On the precepts of the "best good for the greatest number," radium seems to be the method of choice. And as to the matter of how far gland involvement can be conquered by deep X-ray therapy, judgment must be deferred.

It must, however, be admitted at once that it is fallacious to believe that it is fair to compare favourably the 50% five-year cure obtained by radium in cases in Stages I. and II. with the figure of (approximately) 40% obtained by surgeons in their operable cases. For the surgeon tries to call as many cases operable as possible and an operability rate of 60% or thereabouts is frequently claimed. But the radiotherapist does not include anything like 60% of his cases in his Stages I. and II. His figures are much lower.

*Percentage of Cases included in Stages I. and II.*

Gray Ward and Sackett . . . .	20.5%
Pitts . . . . .	28.5%
Heyman (1920-1928) . . . .	41.8%
Collected figures . . . . .	31.0%

Therefore the two groups of cases are thus not really comparable. When the radium therapist claims to produce 50%, 60% or more cures in Stages I. and II., he is getting this high percentage of cures out of the very early cases, which amount to perhaps 30% of all the cases he sees. The operating surgeon only gets, roughly speaking, 40% five-year cures; but he cures this percentage out of a larger fraction of the total number of cases seen by him, *i.e.*, up to 60%. His group of operable cases must, therefore, be considered roughly to include Stages I., II. and a good many cases classified as Stage III, in most of the figures published from clinics where radium is used.

It will at once be realised that the following is only an approximation, but it may serve to clarify the position :—

A surgeon skilled in the performance of the Wertheim operation may hope to get 40% five-year cures of the cases he operates on. If his operability rate is 60% then of every 100 cases seen he "cures" 40%, or two-fifths of 60. *i.e.* 24. To this may be added, say, the one case saved by radium therapy from the cases rejected as inoperable, so that the total salvage by operation treatment for the operable cases and radium for the inoperable is 25 out of every 100 cases seen.

We now turn to the consideration of what can be done by radium. with nowadays the probable reinforcement of X-rays. It is no unusual thing for a clinic to be so successful as to have 60% five-year cures of its cases in Stages I. and II. But these cases may only constitute some 30% of all cases seen. In other words, of every 100 cases seen, 30 are in Stages I. and II., and of this 30, 66%, or 20 cases, are five-year cures. To this must be added, say, another 5 cases, representing the cases "cured" from among the remaining 70 of the original 100 cases and which were classified as belonging to Stages III. and IV. The total salvage by radium and deep X-ray, therefore, also appears to be about 25 out of every 100 cases seen.

A concrete example may be selected. Reference to the table of the results reported by Dr. W. P. Healy (p. 159) shows that of 159 cases seen, only 35 or 22% were classified as Stages I. and II. Among these 35 cases the relative cure rate is published as 63%. But it only represents a salvage of 13.8 cases in every 100 cases seen. His Stages III. and IV. comprise 106 cases among 159 cases seen or 66.6 per cent. (75.2% of the cases *treated*). In these stages 18 were "cures" which, again stated as a salvage among 100 cases seen, amounts to 11.3. The total salvage per 100 cases seen is thus, of course, the same as his "absolute" cure rate, *i.e.*, just over 25%.

Again it must be emphasised that the above outline of the situation is only an approximation but 25% would seem fairly to represent the five-year average cure obtainable at most clinics. And certain hospitals, *e.g.*, the Marie Curie, claim vastly better results. At the same time it must be agreed that most gynaecological surgeons will *not* be able to operate on 60% of all cases seen and will *not* get such good end results as the 24.6% absolute cure rate claimed by Bonney.



So the statement made elsewhere that radium can do everything that operation does for the cure of cancer of the cervix, and, what is more, do it without the high initial mortality rate, still holds good in the light of our present knowledge and with particular reference to a cure standard of five years. Whether or not the ten-year radium figures will bear the same favourable comparison with the ten-year operative results still remains to be seen. From such evidence as is available up to the present it would seem doubtful if the radium results will then appear in quite such a favourable light.

There remains, however, one more point. Certain women must never be allowed to guess they have cancer. They may perhaps be subjected to a radical operation for this condition without having any suspicion aroused in their minds. But if they were to receive three applications of radium and then a course of deep X-ray therapy they would be left in the complete and miserable certainty of the true knowledge of the complaint from which they were suffering.

Against this may be set the fact that radium therapy does not affect the patient very seriously. Many patients are able to work even between treatments and generally within a short time of its completion. This is not quite true if deep X-ray treatment is also given. That often has a profound general effect during its administration and for a considerable time afterwards. But even here, the incapacity for work is not so long as in the case of patients who have been subjected to surgery.

### Details of Technique of Radium Therapy

There is no finally settled technique for the treatment of carcinoma of the cervix by radium. The differences depend largely on whether the principle of giving a relatively small dose of radium over a long continuous period of time is accepted; or whether, instead, a large dose over a short period of time is considered preferable. The latter mode of treatment is exemplified by the technique worked out by Forssell in 1914 and practised with little variation since then at the Radium-hemmet at Stockholm.

**The Stockholm Technique.** Contact radium treatment (brachy-radium treatment) is concentrated into two or three applications given during the course of a month. Relatively large amounts of radium are used, the applications being applied simultaneously in the uterus and vagina. The filtration is heavy, being the

equivalent of 3 mm. of lead. Heyman (11) prefers to give three treatments, the second being given one week after the first, and after a further three weeks' interval the third treatment would be given. A typical treatment series would be:—

In the uterus 40 mg. el.  $\times$  20 hours = 800 mg. el. hours.

In the vagina 75 mg. el.  $\times$  20 hours = 1,500 mg. el. hours.

One week interval.

Second treatment—same dosage.

Three weeks' interval.

Third treatment—same dosage.

Thus the uterus receives 2,400 mg. el. hours and the vagina 4,500 mg. el. hours. The filtration is by platinum equivalent to

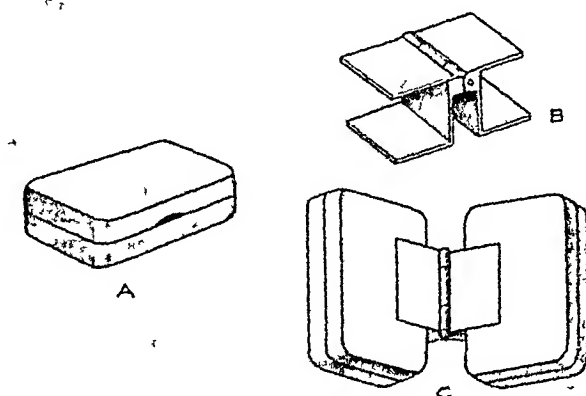


FIG. 25. A. Flat box container for radium needles; B. Clip fastener; C. Boxes articulated by means of clip fastener (after Heyman).

1 mm. lead in the walls of the radium containers and metal equivalent to 2 mm. lead in the applicators. The variety of applicators available at the Radium-hemmet is described by Heyman (*loc. cit.*) and in greater detail by Thoracius (12). The applicators receive a further covering of rubber and oiled silk which serve to screen off the secondary radiation.

The difficulty in finding sufficient beds and radium for an increasing number of patients has forced a change in the above technique, and for many years most cases treated at the Radium-hemmet have received only two treatments with a three weeks' interval. Such a concentrated treatment demands a decreased dose, and in this technique the average total in the uterus is 2,200 mg. el. hours and 4,000 in the vagina. The above dosages

are rarely exceeded, largely because of the fear of injuring the rectum, even if this be pushed as far from the radium as possible by plugging. The dose may, however, be increased as an exceptional event if the radium has to be spread over a large area on account of the size of the tumour. Scraping away the mass of the tumour is never done (*cf.* Paris technique). The dose is not varied according to the histological character of the tumour:

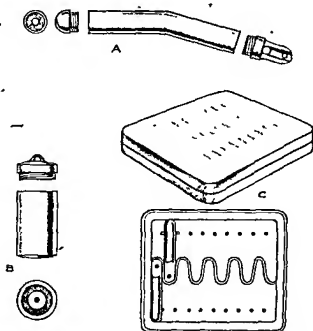


FIG. 26. A. Intra-uterine radium applicator; B. Cylindrical applicator for vaginal use, C. Flat box applicator of larger size than in Fig. 25 (after Heyman).

squamous cell and adeno-carcinoma of the cervix receive the same radiation.

The large variety of applicators which are available at Stockholm and the method of selection for each particular case has two objects. One is to cover as far as possible the entire vaginal surface of the tumour and the other to distend the vagina laterally so that the radium comes as close as possible to the lateral pelvic walls (Figs. 23, 26, 27).

In addition to the brachy-radium treatment, X-radiation to anterior fields, and, in advanced cases, two posterior fields is also employed, but as already stated, Heyman is not convinced of its great value. More recently tele-radium treatment by a gm. "bomb" has been employed and may perhaps be viewed more optimistically.

Finally with regard to the technique of the actual application, the day before the intended treatment the patient receives an

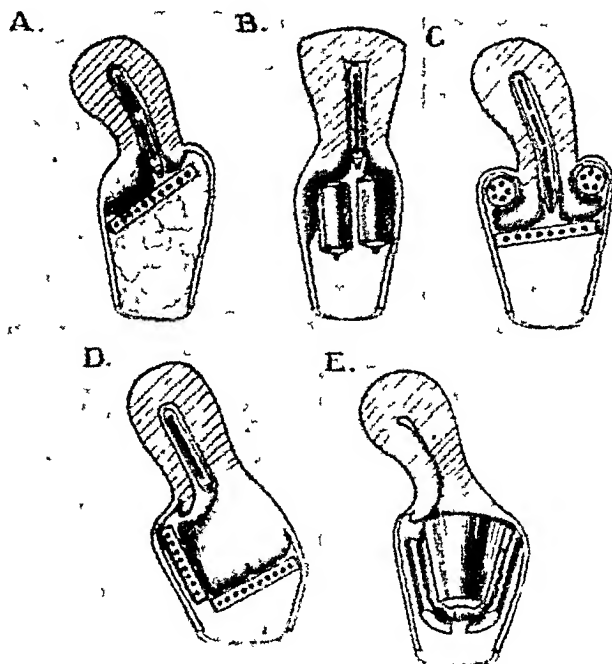


FIG. 27 Some of the applicators available at the Radium hemmet adjusted so as to treat various shapes of growths. (After Heyman.)

enema and a vaginal douche. Vaginal packing has now been abandoned.

On the day of the treatment a hypodermic injection of morphia is given (only on rare occasions is a general anæsthetic employed) and examination and treatment are carried out at the one sitting. The examination includes cystoscopy as a routine.

The surface of the tumour is cleansed with benzene, the cervix is dilated and the intra-uterine applicator placed in position.

A piece of the growth is then removed with the curette for microscopic examination. The selected vaginal applicators are placed in position and held there by a vaginal plug. We should like to draw attention to what is, in our opinion, a common failure in the technique of those who employ the Stockholm treatment in this country. And that is, that they do not insert the plug nearly tightly enough nor in sufficient quantity to force the vaginal applicators far enough out towards the lateral pelvic walls.

The effects of radium on the blood are observed, and the dosage may have to be reduced in the later applications if certain changes are noted—particularly a leucopenia with a relative lymphopenia.

Cases of recurrence are treated either by needling, by surface applicators or by removal by diathermy.

**The Paris Treatment.** The treatment carried out at the Institut du Radium at Paris is well described by Lacassagne (13), and a modification in technical detail by Swanberg (18).

The principles of the Paris (Regaud) technique are :—

1. Proper preliminary treatment by antiseptic douches with chloramine solution for several days.

2. Small doses over a long period, *e.g.*, 60 to 70 mg. for five or six days. Total radiation rarely exceeding 8,000 mg. cl. hours.

3. Employment of multiple centres of radiation, *e.g.*, one centre for every 2 or 2.5 cm. Therefore usually three centres are introduced into the cavity of the uterus.

4. Heavy filtration, 1.0 to 1.5 mm. platinum or its equivalent.

5. The use of external radiation in addition to intra-uterovaginal when the growth has extended beyond the uterus.

For an average case four tubes of 13.33 mg. and two tubes of 6.66 mg. radium element are employed, each tube being 20 mm. long, the radium occupying the middle 15 mm. These tubes are arranged in two sets of three, each set consisting of two of 13.33 mg. and one of 6.66 mg. One set is used in the uterus and one in the vagina.

The patient to be treated is admitted to hospital, and obvious sepsis is cleared up as far as possible by douching, etc. When this is achieved, the cervical canal is identified and gently dilated. Should this cause no rise of temperature, the next day the radium is applied following a second gentle dilatation of the cervix.

The set of tubes for the uterus (Fig. 28, *a, b, c*) have walls of 5 mm. of platinum. The three tubes are placed in a rubber eath having walls 1.5 mm. thick to screen off secondary diation, and the whole is introduced so as to occupy the entire ngth of the canal of the uterus and cervix.

The vaginal tubes have walls of only 1 mm. of platinum. The wo larger tubes (13.33 mg.) are inserted in a simple spring

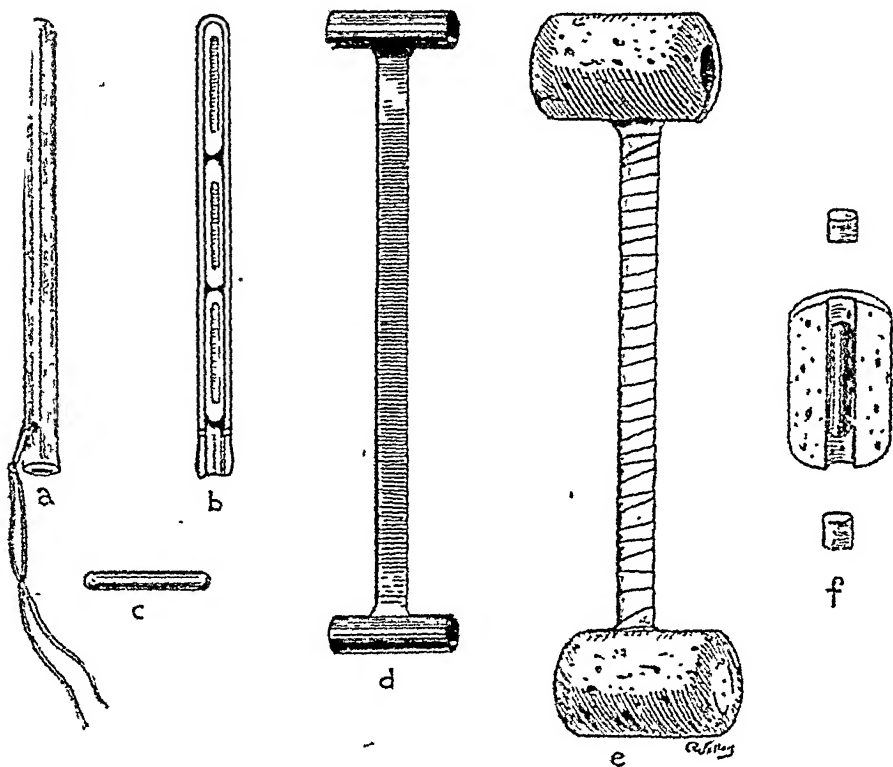


FIG. 28.

apparatus called a "colpostat" (Fig. 28, *d, e, f*), and in this they receive a secondary screenage of 5 mm. of cork which has been rendered impermeable to vaginal secretions by collodion. When the "colpostat" bearing the radium is properly introduced the applicators rest one in either lateral fornix. Their long axes are in the sagittal plane, and they are forced as far apart from each other as is possible, by the spring of the apparatus. The third tube, with a similar cork screen, is made to lie in contact with

the cervix being held in place in the concavity of the spring (Fig. 29).

The total duration of the radium application is five days, and at the end of each twenty-four hours all the applicators are removed, cleaned and replaced after douching the vagina.

If the uterine canal is not permeable, the vaginal application alone is employed for two or three days, and at the end of this time it is usually possible to identify the canal and safely to dilate it. After that, the intra-uterine radium is applied.

This treatment is later supplemented, in all but Stage I. cases, by deep X-ray therapy or by distance radium therapy by means of a "bomb."

In the "bomb" method 4 gm. of radium element in a box with walls of 6 cm. of lead is employed at a minimum distance of 10 cm. from the skin. In the average case eight fields are irradiated: two anterior, two lateral, two posterior and two posterior-inferior. Sometimes a perineal field is added. The full exposure is for about ten hours through a screen of 1 mm. platinum to each field. Only one of the fields is treated

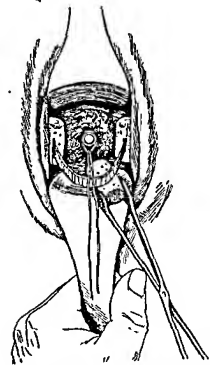


FIG. 29. Method of applying vaginal radium in the Paris technique. (After Lacossagne.)

each day, and different fields on successive days. The first exposure is for three hours, the second for three hours and the third for four hours. Thus it takes twenty-four or twenty-seven days to complete the full course, and during all this time the patient is in hospital.

If deep X-ray therapy is employed, a similar technique is followed, but the fields irradiated are larger. The applications are given for at least one hour twice daily, different fields being

treated. The total time for exposure for each area is five to eight hours, and the full course occupies fifteen to twenty-five days, during which time the patient is not confined to hospital.

The modified applicator suggested by Swanberg is a T-shaped tube

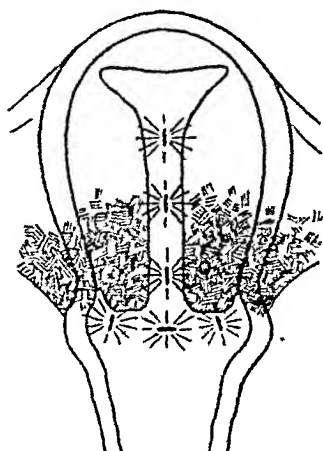


FIG. 30. Centres of maximum radiation and (shaded) approximate area of tissue effectively radiated. (After Swanberg.)

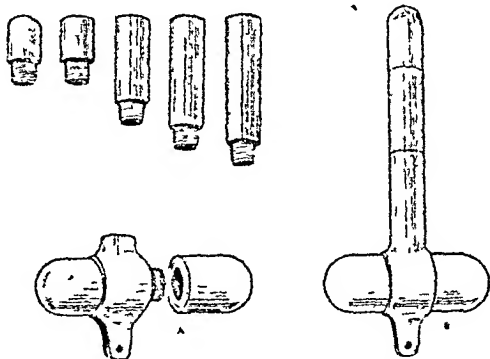


FIG. 31. Applicators for combined intra-uterine and para-cervical radiation. (After Swanberg.)

(Fig. 31) which can be adjusted to fit any uterine canal from 1.5 cm. to 10 cm. long and in which one to five centres of radium can be fitted into the stem. The vaginal cross-arm can receive one or

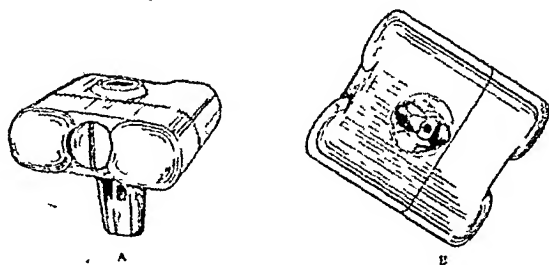


FIG. 32. Another variety of cervical applicator. (After Swanberg.)

two centres according as to whether it has a single-barrelled cross-arm or a doubled-barrelled head (Fig. 32). The average treatment with Swanberg's applicator is by four centres, three in the uterine stem and one in the vaginal cross-arm. Two additional centres are



applied to the fornices either by the "colpostat" or by bakelite applicators as used in the Radium Institute of London (see Figs. 33, 34).

The supplementary radiation by high voltage X-ray (200,000 kv.) may conveniently be given during the preliminary period of douching.



FIG. 33. Vaginal applicator as used at the Radium Institute in London.

total dosage (8,000 mg. el. hours) smaller quantities of radium are employed, usually 10 to 20 mg. in the uterus and cervix and 30 mg. in the vagina. The screening employed is 2 mm. platinum, and rubber. The tubes are removed and cleaned and the vagina douched every one or two days. If there is any difficulty in dilating the cervix they postpone intra-uterine treatment and are content for a few days to apply surface radiation to the growth.

Prior to this or sometimes subsequently Max Cheval recommends distance radiation by a 4-gm. "bomb" of radium employed at a distance of 16 cm. from the skin. Four ports of entry are used and six to ten treatments given.

In Great Britain there is a general tendency to follow the Stockholm technique fairly closely, though special applicators (see Fig. 35) may here and there be introduced as a modification. Generally speaking, however, it can be taken that the results obtained in this country are the product of the Stockholm technique supplemented more and more in recent years by deep X-ray therapy.

The widespread distribution of radium among many institutions in the country is presumably inevitable, but it does lead to the

The technique followed in Brussels is similar to that used in Paris, though the treatment is spread over a longer period of time, up to twelve days, so that to produce the same

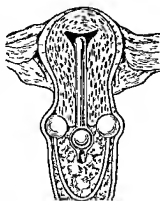


FIG. 34. Intra-uterine and vaginal applicators in position. (After Swanberg)

employment of radium by very large numbers of operators who have no special experience or knowledge of technique, and also who are deprived of the assistance of an expert physicist whose advice on dosage and distribution would be invaluable. If improved results therefore are to be obtained, one step in the right direction would be the establishment of teams in which the gynaecologist receives the help and advice of the physicist, the pathologist and the X-ray operator.

**Abdominal Implantation of Radium.** In the earlier editions of this book a considerable amount of space had to be given to the consideration of the value of this method of treatment. Nowadays this therapy has fallen into disuse and needs no further discussion.

The whole tendency of recent years is, instead, to attempt to treat possible distant lymphatic spread either by tele-radium by means of a 5-gm. or smaller "bomb" or to use deep X-ray therapy. In this deep therapy the usual tube employed is run at 200 kv., though some institutions use a voltage of nearly a million. It is as yet too early to assess the value of these super-voltage-treatments. The more usual 200 k.v. treatment is, as has been indicated in a previous section, become more and more a part of the routine treatment of cancer of the cervix as a supplement to contact radium. Only in a very few clinics is any attempt still made to treat this condition by X-rays alone.

Before leaving this point - a few more figures, after Kamperman (28), may perhaps be quoted. They show a steady improvement in the results obtained at the Harper Hospital, Detroit, corresponding to adjustments in the technique. In all 636 cases were treated. During the period 1922 to 1928 the radium dose was 3,600 to 5,000 milligramme-element-hours. In addition heavy X-ray dosage at 200 k.v. with 1 mm. copper filter was

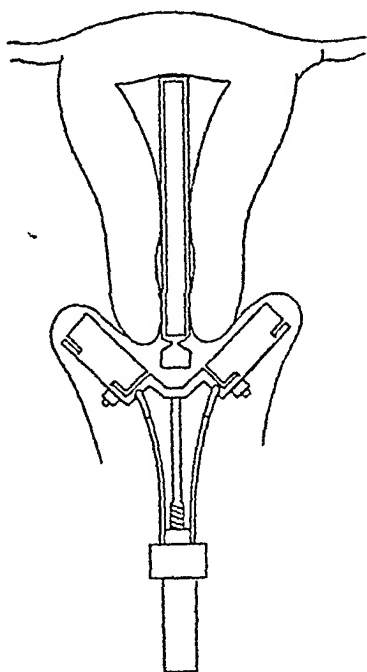


FIG. 35. Vaginal applicator of the butterfly pessary type as used at the Mount Vernon Hospital.

employed. The "absolute" five-year cure rate was 16% and the "absolute" ten-year rate 12%.

From 1928 to 1932 the radium dosage was increased to between 7,200 and 10,000 m.e. hours and correspondingly less X-rays, still at 200 k.v., was used. The absolute five-year cure rate for this period was 21% and the similar ten-year rate had improved to 15%.

Since 1932 the radium dosage had remained unchanged but the quality of the X-rays had been altered to "super voltage" at 500 to 600 k.v. with a filter of 7 mm. copper. Only two years of five-year results of this present therapy were available and the average for this period was 35%.

The suggestion is therefore that this high k.v. X-ray treatment is an improvement. But we await other results.

### The Relative Malignancy of Cancers

Broders at the Mayo Clinic classified cancers, cervical and others, into grades of malignancy according to their histological character. His classification is referred to by Healy (16) who emphasises the important prognostic value of the histological characters of various cancers. In the classification of Broders, Grade I. represents the adult highly differentiated type of epidermoid cancer. Grade IV. comprises the very cellular tumour which is made up of completely undifferentiated embryonic or anaplastic cells. Grades II. and III. occupy intermediate positions.

Grade IV. (malignancy), though highly malignant, is stated to be very radio-sensitive, and therefore much more amenable to radium treatment than to surgical attack. Healy states that of early cases in this group 66% remained well for five years with efficient radium therapy. Maliphant (17) follows Martzloff in dividing epidermoid cervical cancers according as to whether the predominant cell was of the "spinal," "transitional" (commonest) or "spindle." Roughly speaking, he finds that the more highly differentiated "spinal" cell tumour is less malignant and is most amenable to surgical treatment. The "spindle" -celled tumours, though very malignant, are relatively susceptible to ray-therapy and, at least as regards the immediate response, do well under such treatment. Lacassagne (13), however, suggests that the variance in degree of radio sensitivity between the two extremes seems to be less in the case of cervical cancer than obtains in carcinoma of other parts of the body. And this view would appear to coincide with that of the majority of gynaecologists. There does not appear to be any great practical

difference in the results obtained in the treatment of the various histological types of growth. Warren and others (18) express the matter differently. They say that the histological grade of a given cancer is of less importance than is its clinical classification and its response to therapy. They maintain that the guide to the radium sensitivity or resistance is the response in the tumour cells or the stroma to radiation. If the changes are not well marked they suggest that operative treatment should be adopted.

### Early Diagnosis

A good deal of attention has been paid in recent years to the question of early diagnosis of cancer of the cervix or of precancerous conditions such as leukoplakia. Inspection of the cervix by a viewing instrument such as Hinselmänn's colposcope, which gives a tenfold magnification, has been used more extensively on the Continent (Laffont and others (19)) than in this country. Much the same may be said about the test with Lugol's iodine solution. Healthy vaginal and cervical epithelium in contact with this solution will take a dark brown coloration owing to its contained glycogen, whereas cancerous and precancerous tissues remain relatively unstained.

These tests are, of course, performed in this country, but the general opinion would appear to be that the ordinary tests for friability are sufficient for a sure clinical diagnosis in most cases. But if there is the slightest doubt about any given area, the safest thing is to have a portion excised and examined histologically.

## SECTION II. CANCER OF THE UTERINE BODY

It has for years been the accepted view that surgical treatment for carcinoma of the body of the uterus gives such good results that hysterectomy and not radiation is the correct treatment.

But attempts are made from time to time to improve the technique of radium therapy for this disease.

Admittedly, Lacassagne, some years ago (20) came to the conclusion that fundal carcinoma treated by radiation responded so badly, that he believed that these cases should be treated by surgery until a better radiation technique than he was then employing should have been evolved. Regaud appeared to agree and to think that carcinoma of the corpus is relatively insensitive to radiation.

But in America, in Germany, in Great Britain and in Stockholm

new methods are on trial and an attempt must be made to compare the new results of radiation with those obtained by surgery. Of the many published figures for the latter, perhaps the best known are the combined figures published by Lane Claypon in 1927 (21)

The total number of cases considered was 507. Of these 80.7% were operable and had abdominal hysterectomy performed with 6.4% operative mortality. The five-year cure rate was 60%.

With these figures for comparison we can now study the technique and results of some of the clinics employing radium therapy usually in combination with deep X-rays. The question

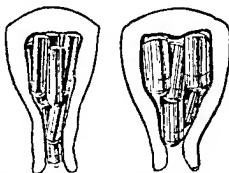


FIG. 36. Uteri packed with many applicators. (After Heyman.)

receives further consideration in the Chapter devoted to "X-ray Therapy in Gynaecology."

The present *Stockholm* treatment is to pack the uterine cavity with a large number of applicators containing relatively small doses of radium. The total quantity of radium used varies between 80 and 200 mg. el., but the total dosage, distributed in two treatments, lies between the limits of 2,600 and 4,000 mg. el. hours. Then because of the danger of later metastasis to the vagina at least one vaginal treatment is given.

In discussing the results Heyman (22) excludes those cases of adenocarcinoma involving the cervical canal and the corpus (a group of cases to which a great deal of attention has been paid at many centres in recent years) and which he describes as "Carcinoma corporis et colli uteri." He excludes as well those cases in which ovarian cancer is also present and reports on the results of treatment of 460 cases of "carcinoma corporis uteri."

Of those treated five or more years ago :—

Total number of cases examined	232
Symptom free after five years	98
Absolute cure rate	42.2%

but this figure includes cases treated by surgery combined with adiotherapy because the latter seemed to be a failure.

Of the cases treated only with radium. *i.e.* counting the cases operated on as having died :—

Number of patients treated	224
Symptom free after five years	74
Relative cure rate	33.0%

He quotes figures from published statistics of large series of cases giving the results of operative treatment in which the five-year cure rate is not as high as in Lane-Claypon's figures. He finds the average "absolute" cure rate is 41.7%, while the average relative cure rate (cases operated on) is 50.9%. However, these figures are not really comparable, as the cases operated on must contain a good number of early cases, while Heyman's series treated by radium contained 17.4% inoperable cases and a further 44.6% unsuitable for operation for other reasons. It is therefore again extremely difficult to compare the results of the two kinds of treatment.

In *America* the tendency is to use radium plus X-rays with in some hospitals a very high voltage; or to combine radiation therapy with hysterectomy. Thus Healy and Brown (23) report 197 cases treated at the Memorial Hospital among which 96 were treated by radiation alone and 93 by radium plus surgery. The latter group had a five-year survival rate of 55% which compares favourably with the 39% obtained by radium treatment alone. In the cases treated by radium alone the prognosis was markedly affected by the extent of the growth. If the uterus were less in size than a two and a half month's pregnancy then the five-year survival rate was 56%. In 7 cases in which the uterus was bigger than this there were no five-year survivals. These writers advise removal of the uterus preceded by adequate radiation. Yet they hardly seem to have made out a good case for radiation therapy as their cases subsequently show an unduly high incidence of fistula (which may presumably be attributed, at least in part, to the radiation), and their results cannot be said to be overwhelmingly good. Their technique is to place two or three

radium capsules in tandem in the uterus and to allow them to remain until 3,600 millicurie-hours dosage have been administered. Two weeks later deep X-ray therapy is given through four ports of entry. Six to ten weeks later, hysterectomy is performed during which the imbricated ends of the tubes are ligated as a preliminary step. Kamperman (24) reports the cases at the Harper Hospital, Detroit. Although the figures are small they deserve quotation because they do point to the possibility that combined ray-therapy and hysterectomy may eventually prove to give the best results.

*Table showing Five-year Results in Operable Cases of Carcinoma Corporis. (After Kamperman.)*

Method of Treatment	Cases treated	Well after five years	Percent
Hysterectomy and post-operative radiation . . . . .	36	20	55
Pre-operative intra-cavitary and external radiation, hysterectomy six weeks later, then post-operative X-rays . . . . .	7	5	71
Total . . . . .	43	25	58 = relative cure rate

He also reports on 34 inoperable cases treated by radiation therapy alone with 10 five-year survivals, or 29%. But it is probable that quite a number of cases of carcinoma of the body of the uterus would survive five years and would be without any very grave deterioration, even if untreated. This possibility should be borne in mind when assessing five-year "cures" of corporeal cancer.

The question whether radium therapy should supercede operation must, however, be given very serious attention when under no less an authority than the Medical Research Council "Summary of Reports from Research Centres" for 1937 appears the statement that "an analysis of the radiologically treated cases . . . suggests that radiotherapy may be the best method of treatment for most cancers of the corpus. . . ." The Report proceeds to suggest that 42% would represent the absolute cure rate for surgically treated cases. For comparison with this, the figures from the Marie Curie Hospital are quoted.

Marie Curie Hospital

*Cancer of the Corpus Uteri. Five-year Survival Rates among Cases treated between October, 1925, and December, 1932*

Stage.	No.	Five-year survival rate.
Operable . . . . .	7	7 = 100 %.
Clinically inoperable . . . . .	33	18 = 54 %.
Technically inoperable . . . . .	27	4 = 14.8 %.
Total . . . . .	67	29 = 43.2 % = relative survival rate.
Total number examined with a view to treatment	69	29 = 42.0 % absolute survival rate.

It would appear that this absolute survival rate is thus the same as the absolute cure rate for the surgically treated case (see p. 184).

An objection to this conclusion is the feeling that will be present in many people's minds that the figure for surgery is too low. Yet it is almost exactly what Heyman (*vide supra*) said was the average of the surgical figures he had collated !

The next argument may be that the radiation figures are only from the hospital that makes a habit of producing the highest or nearly the highest cure rates in the world ; and that other hospitals or individual care can hardly hope to do so well. But this again is not borne out by figures. The next table, which gives the collected results from seven different radiation centres, shows that other places do get the same results.

*Carcinoma Corporis Uteri Collected Results from Seven Reporting Centres in Great Britain*

Cases treated in 1932.	Living five years later.	Dead.	Five-year relative survival rate per cent.
32	14	18	43.7

So the fact that most gynaecologists will continue to treat these cases by surgery can be attributed to conservatism if so desired. But it would be fairer to say that they will be watching with interest to see what transpires when larger numbers of cases have been treated and when longer periods of time have elapsed between the application of the radium and the acceptance of the case as cured.



A possibility that may meet with more ready acceptance is that radium and X-ray therapy may make a valuable complement to surgery. Some figures showing the results of treatment of these cases at the Women's Hospital, New York, and kindly supplied by Dr. Sackett in a personal communication supports this suggestion.

*Results of Treatment of Carcinoma Corporis Uteri*  
(After Sackett)

	No	Living 5 years.	Survival rate per cent.
Total cases seen . . . . .	142	63	Absolute 44.4
Untreated . . . . .	9	0	0
Treated . . . . .	133	63	Relative 47.4
Surgery alone . . . . .	27	17	Relative 63.0
Radiation alone because case inoperable or because operation contra indicated.	69	22	Relative 32.0
Radiation and surgery . . . . .	37	24	Relative 64.9

We may conclude that it is probable that most gynecologists will require a lot of persuasion before they will accept the above-quoted statement from the Medical Research Council's Summary of Reports. The value of radiation therapy as a *supplement* to surgery would seem at the moment to be a more valuable subject for inquiry as most cancers of the uterine body will—at least for a considerable number of years—continue to be treated by hysterectomy.

### Technique .

The methods used in the radiation treatment of this disease demand attention because there are always inoperable cases or cases in which operation would be contra-indicated, and for such cases this form of therapy is plainly desirable. Furthermore, continued research may show that the value of ray therapy will become so evident that the most conservative of gynecologists will be converted.

As an example of a well-tried technique may be cited the one employed at the Marie Curie Hospital and published by Hurdon and Chambers (25). They divide the radium dose into three applications of twenty-two hours each, given at one and then two weeks' intervals. The distribution of the radium is intra-uterine and vaginal (Fig. 37). The screenage of the uterine radium is

1 mm. platinum and 2 mm. rubber. In the vagina 0.3 mm. platinum, 2 mm. silver and 1.5 mm. rubber is used. The total intra-uterine radium varies from 50 to 78 mg., while the vaginal plaques each contain 20 mg. Of recent years the radium treatment has been supplemented by deep X-rays.

### Histological Grading of Malignancy

Just as in cases of cervical cancer, it has been suggested that the microscopical picture can assign any given tumour to its grade of malignancy. Healy (26) divided the tumours into four grades, Grade I. being the most differentiated and least malignant; Grade IV. being the least differentiated but most malignant—also the most radio-sensitive.

Crosby and Henderson (27), however found that grading from scanty material removed for biopsy was unreliable, in that a diagnosis of, say, Grade II., may be made from the curettings, while the tumour after removal may show that it should have been classified as Grade IV. In these series of cases the grade of malignancy did not have any prognostic value and therefore was of no value in determining which cases were theoretically more suitable for radiation therapy than for surgery. Furthermore, there were variations in the grade of malignancy in different parts of the same tumour. Also a seemingly mild primary tumour was capable of giving rise to anaplastic and extremely malignant (microscopically) secondary growth.

The conclusion would appear to be that there does not seem to be much value in the attempt to grade cases of carcinoma of the uterine body on their microscopical appearances.

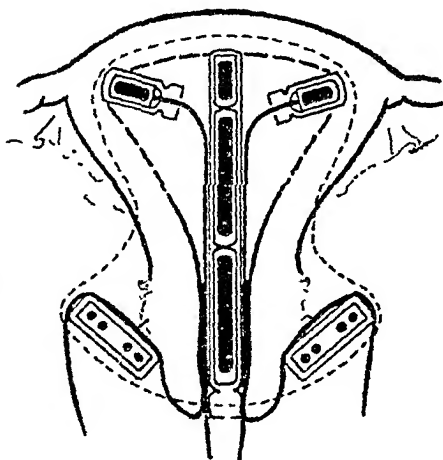


FIG. 37. Intra-uterine and vaginal applicators in position for treatment of a case of carcinoma of the body. (After Hurdon and Chambers.)

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## CHAPTER IX

### STERILITY

WHEN we remember the complexities of conception, our wonder should be placed rather on the frequency of its successful accomplishment than on its occasional failures. The formation of spermatozoa, the phenomenon of ovulation, co-ordinated with tubal activity and uterine changes by an elaborate chemical system, in addition to the mechanical act of coitus, all timed and designed to ensure the fertilisation, embedding and the later development of the ovum, together form the most marvellous of all the processes of life.

It is obvious, therefore, that continued failure to conceive may involve one or more of so many possible defects in conditions as yet little understood, and it provides us with a pathology of sterility which presents problems of the greatest difficulty. During the last few years, however, much progress has been made in our knowledge of some of the details of endocrinology and other aspects of reproduction, which has enabled us to treat sterility with more understanding and hope of success. In the present chapter we shall confine ourselves to discussion of female sterility only, with special reference to the physiology of ovulation, fertilisation and the progress made in certain forms of treatment.

**Ovulation.** The broad facts of the maturation of the follicle, and dehiscence of the ovum have been known for many years. The general idea of rhythm in ovulation and menstruation have associated the two phenomena in such a way that we have hitherto regarded the two as closely interdependent, but clinical anomalies and animal experiment have now made it clear that, though there is a loose connection, yet the two are actually separate processes.

The ripening of the follicle is controlled by one of the gonadotropic hormones, secreted by the anterior lobe of the pituitary body, but it is yet uncertain whether the final turgescence and rupture of the follicle with liberation of the ovum is due to continued action of the pituitary, or the influence of œstradiol, a hormone which is secreted partly by the non-follicular tissue of the ovary. The successful production of fertilisable ova is perhaps the most fundamental of all the essentials in the chain of events which ultimately produce the full-term child, but in any given case of sterility, where obvious pathology is absent, it is almos

if not quite, impossible to state whether or not the ovary is producing normal ova. Experimental work suggests that ovum formation is due to the action of the pituitary hormone, but we have not yet been successful in isolating this specific hormone in doses which will have a therapeutic effect on women. While it is known that follicles can be made to mature by the influence of the follicle-stimulating hormone (prolan A) of the anterior pituitary, yet these follicles need not necessarily contain ova. For example, if prolan A be injected into immature rats the ovaries will develop a number of follicles, but they will not contain ova.

Apart from the mechanism of the ripening and rupture of the follicle, we do not yet know whether there is any monthly regularity in the production of an ovum. In some women there may be long intervals between the production of normal ova, or in others it may be that not all regularly produced ova are fertilisable. Endometrial biopsy may show evidence of ovulation by the appearance of the secretory (luteal) phase, but examination of the same woman during another cycle may show no secretory appearance.

Conception depends not only on the production of an ovum, but on the time it is produced during the monthly cycle in relation to coitus. There is much evidence to show that ovulation occurs in four-fifths of all women on or about the thirteenth day after the first day of the last menstrual period. Coincident with the rupture of the follicle is the maximum output of oestradiol in the urine and also of the mucus secretion from the cervix (Séguy and Simonnet) (1). There is also much supporting evidence from the inspection of the ovaries during laparotomy at various dates of the cycle.

Knauss and Ogino (1929 and 1930) have stated that ovulation occurs in all women at the middle of their month, and that, as the ovum is not capable of living more than two or three days before fertilisation, there is a sterile period of about a week before the first day of the next period. This statement is of obvious importance, because, if true, it means that there is a natural method of control of births without complete abstinence or artificial devices. For the majority of women it is true that usually ovulation occurs between the twelfth and sixteenth days, but it is not true of all women, and also not every woman ovulates regularly on the same date of each month. Reliance, therefore, on the "safe period" is liable to be betrayed, and sooner or later will be followed by disappointment.

Devraigne and Seguy (2) have critically examined the theory of Knauss and Ogino. They point out that ovulation can exist without menstruation, as shown by the numerous examples of conception occurring during a period of amenorrhœa, and also the converse, that menstruation can occur in the absence of ovulation. Evidence of the latter was given by Bramwell and Parkes (3), who showed that mice who had had both ovaries X-rayed, in order to kill the follicles, still exhibited a normal œstrus cycle.

In human subjects after the menopause, Kaufmann (4) was able to produce menstruation by giving large alternate doses of œstrone and progesterone. The former and generally accepted view was that menstruation was dependent upon the rhythmic formation and death of the corpus luteum, which was the direct result of the ruptured follicle. An apparently firm basis for this view was that, after complete removal of the ovaries, menstruation ceases entirely from that date. We have the experimental evidence given above which shows that menstruation *may* be independent of ovulation, but it is extremely rare to open the abdomen during the childbearing period of life, and fail to find a corpus luteum either active or degenerate.

Our own feeling is that in the very large majority of women, there is a monthly formation of a corpus luteum upon which menstruation is either directly or indirectly dependent. Where menstruation occurs in the absence of ovulation, it is possible that the luteal hormone (progesterone) may be elaborated by the non-follicular tissue of the ovary. We know that these cells are able to produce the follicular hormone. The corpus luteum is the direct result of a ruptured follicle. But does every ruptured follicle indicate, *ipso facto*, the liberation of a normal ovum? We think this is an assumption for which, as yet, there is insufficient evidence. Some women may produce a normal ovum from every follicle that is ruptured, while others may only at rare intervals, or indeed never, develop an ovum that is capable of fertilisation.

It is certain that ovulation *can* occur at any time during the month. Schikele, during the course of twenty-five laparotomies, found that the follicle ruptured twelve times from the first to the fifteenth days, six times from the fifteenth to the twentieth days, once on the twenty-first day, and once on the eve of menstruation. His observations led him to believe that there is no strict association between the corpus luteum and menstruation. The subject has been fully examined by Hartman (5) in a

recent book. He gives the evidence of pregnancy following a single dated coitus and other evidence based upon hormone levels in urine and blood, the cyclic changes in uterine motility as worked out by Knauss, inspection of the ovaries at the time of operation, and the appearance of the "vaginal smear."

We may sum up then the present state of knowledge of ovulation. The follicle matures and ruptures under the influence of a hormone from the anterior lobe of the pituitary gland. It is probable also that this same hormone stimulates the simultaneous secretion of oestradiol by the follicle and interstitial cells of the ovary. Menstruation and ovulation are essentially independent phenomena, but in most women the follicle ripens after menstruation ceases, and ruptures during the middle of the month, while the degeneration of the corpus luteum is followed by the next menstrual period. Menstruation and ovulation can occur each without the other. Ovulation can occur at any date in the cycle, and in one-fifth of all women there is no so-called "safe period" during the week before menstruation.

Sterility may obviously be due to a failure to produce normal ova, for we have no evidence that every follicle, or even the majority, contain an ovum.

### The Fallopian Tube

Until recently the tube was regarded as a passive duct along which the ovum was propelled by ciliar action.

How the ovum gained the tubal ostium was a mystery, and no adequate explanation had been offered until Westman (6) showed by experiments on monkeys that the tube wraps itself around the ovary and applies its *simbræ* thereto during the time of ovulation. The dehisced ovum, therefore, does not fall loosely away from its follicle, but directly on to the mucous aspect of a *simbria*, whence, by the aid of the cilia, it is passed into the lumen. It is obviously impossible that this remarkable mechanism could be seen during laparotomy owing to the general inhibition of unstriated muscle under the influence of the anæsthetic, nor can it account for conception occurring in those women who possess one tube and one ovary on opposite sides.

The tube is developmentally similar to the uterus. Both are derived from the Müllerian ducts, and we might therefore expect that both would respond in a similar fashion to the same chemical stimuli. Moreover, the tube wall contains two layers of muscle fibres, and it is unlikely that the tube would be incapable of

any active contractile effort. During pro-œstrus and œstrus, the uterus becomes increasingly active, and it is not only a reasonable assumption, but we have evidence that the tube is in an active state of peristalsis during this period. There is the evidence of Westman, given above, and tracings made by the salpingo-kymograph. Rubin (7) and King (8), which show definite peristaltic waves due to tubal activity. The tubal mechanism must play some part in the chain of events which lead to conception, but that it cannot be essential is shown by the occasional pregnancy which can follow complete removal of both tubes, provided the interstitial portion is still open at the uterine cornu. These rare cases prove that the ovum can have direction in its wanderings after it leaves the follicle, but it must be a very small chance, by which, in the absence of the fimbrial grasp of the ovary, the ovum can find its way to the minute orifice at the cornu.

The salpingo-kymograph has given us much more information than is possible by the use of the simple tube insufflator or even X-rays after the injection of lipiodol.

By a study of the graphs obtained by this instrument, it is possible to diagnose normal patency (which should be tested only between the eighth and fourteenth days after the first day of the last period), tubal spasm, tubal stenosis, and complete obstruction. When the tubes are normally patent, 60% of cases allow the gas to pass between pressure of 75 and 100 mm. of mercury; in 23% it passes below 75 mm., and in 7% of cases the pressure rises above 150 mm. King reports that of 145 cases of insufflation, 48% were normally patent, in 2% there was spasm, in 14% stenosis, and 36% were completely obstructed.

There is no doubt that the kymograph tracing is a great improvement on simple insufflation, in so far as it gives much more information, and provides a permanent record for the patient's note file. With one exception, it is also a more desirable method of tubal diagnosis than X-ray examination after lipiodol injection. The exception is that the radiogram will identify the site of the obstruction, knowledge of which is necessary if an operation on the tubes is under consideration. But after the claim for radiography, based upon its power to localise obstruction, has been made, it should be said that the possible dangers of the method render it unsuitable for routine diagnosis of tubal obstruction.

Cases have been reported of oil embolism, but chiefly the objections are due to the occasional failure to absorb the lipiodol



which has leaked into the pelvic cavity. A collection of the oil may become encysted, and give rise to a mild plastic peritonitis, or even a pelvic abscess, which will require subsequent operation. In view of the possible and by no means uncommon sequelæ of

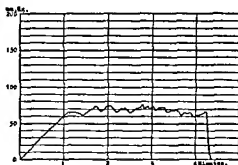


FIG. 38.

lipiodol injection, opinion has swung back towards the original method of Rubin (occasionally combined with a kymograph) as being the safer and better method of tubal diagnosis. Novak (8) advocates a return to Rubin's technique and states that if due

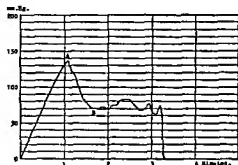


FIG. 39.

care is given to strict asepsis, and if carbon dioxide insufflation is always avoided before menstruation, after amenorrhœa, during any form of menstrual hæmorrhage, and in any patient who might possibly be a subject of pelvic tuberculosis there is no danger in the use of the method.

Insufflation under fairly obvious safeguards is almost entirely

without risk. Here and there a case of air embolism has been reported, but in proportion to the very large number of cases, the risk of accident must be extremely small.

The graphs (reproduced from the published work of King (7))

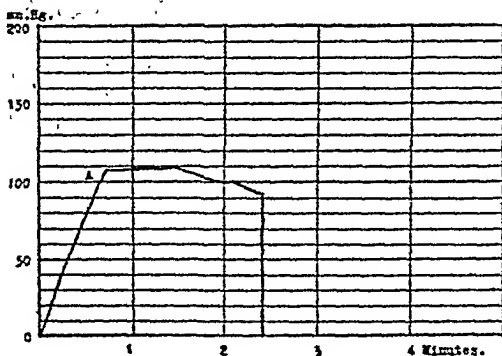


FIG. 40.

indicate the various types of result obtained by the salpingo-kymograph. Fig. 38 is typical of normal tubal patency on the eighth day of the cycle where gas has passed at about 70 mm. The oscillations are caused by rhythmic tubal contraction every

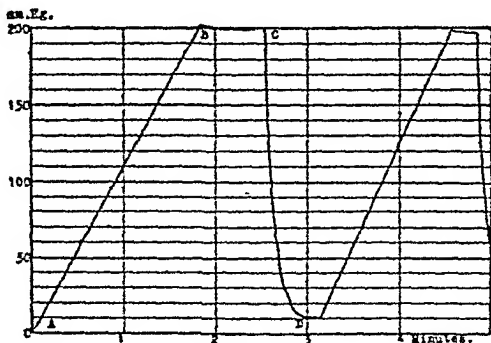


FIG. 41.

few seconds. Tubal spasm is illustrated in Fig. 39. The pressure rises directly to 135 mm., after which there is a sudden fall to 70 mm. The usual oscillations follow while the gas passes without difficulty. Evidence that this type of curve is due to spasm is that, under the influence of anti-spasmodic drugs, the curve takes on the character of a normal tracing.

Tubal stenosis is shown in Fig. 40 where there is a moderate rise to 100 mm., followed by a gradually declining line of pressure as gas slowly filters through the stricture. Complete obstruction is indicated in Fig. 41 where the rise of pressure is carried to the limit of safety without any passage of gas through the tube. After release of the pressure, a further attempt was made to insufflate, without success.

It is uncertain what part tubal spasm can play in sterility. It may be a feature only of the oestral period after rupture of the follicle, when the Mullerian muscle is in a state of tone and readily excitable, or it may be a direct response to the irritation caused by injection of gas under pressure.

The observations of Westman on tubal contractions around the ovary at the time of ovulation suggest that a pathological spasm of the tube, such as may be seen in other unstriated muscle, may be an obstruction to the passage of the ovum, and, incidentally, may be the cause of "middle-pain."

### Fertilisation

We have already made reference to the lack of knowledge on the mechanism of the transference of the ovum from the follicle to the tube. In the same way we have been ignorant until recently of the various factors which facilitate the journey of the sperm from the vagina to the ovum. It will be remembered that the pH value of the normal vagina between puberty and the menopause is between 4 and 5, fairly constantly between 4.4 and 4.6. This is a relatively high degree of acidity, due to lactic acid produced by the *acidophilus bacillus* (Döderlein) normally present in the vagina. The cervical canal, on the other hand, is invariably alkaline, between 7.3 and 8.0 (the neutral point of litmus is 7.3). The seminal fluid is also faintly alkaline, with an average figure of about 7.4 to 7.6. Immediately after coitus the acidity of the vagina is reduced to about 6.2. The reduction is produced not only by mixture with the semen, but also by an increased secretion of the alkaline cervical mucus which normally occurs during the excitement of coitus. But if the orgasm does not occur, presumably the secretion of cervical mucus is deficient, and the pH is found to be only about 5.5 (Séguy and Vimeux (9)). As we shall see, the pH value of the vagina after coitus is of great importance in the mechanism of conception.

The spermatozoa live easily in an alkaline medium of 7.6 or thereabouts. In such a medium, other conditions being suitable,

they will probably survive in the active state for twenty hours. When deposited in the vault of the vagina, they are suddenly surrounded by a fluid whose resultant  $pH$  is 6.2, *i.e.*, on the acid side of neutral. The effect of reducing the  $pH$  of the medium is to render the sperm much more active, but much less able to survive.

In this medium sperms are all dead within an hour, while a slightly stronger acidity kills them at once. If, therefore, the ovum

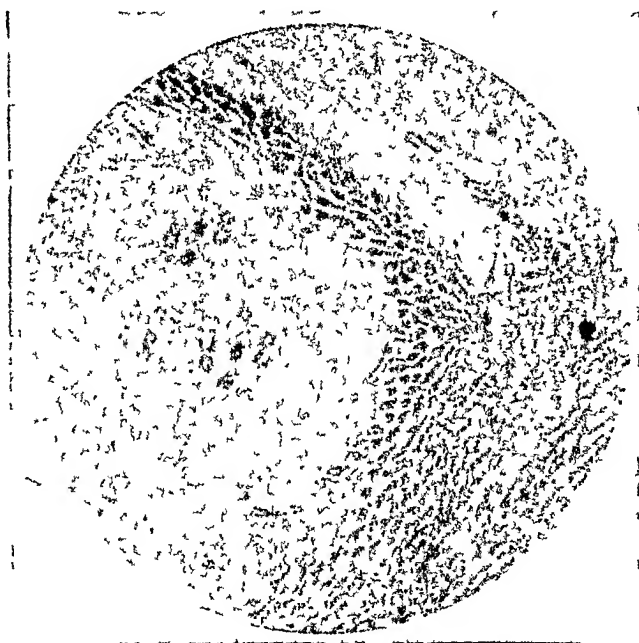


FIG. 42. To the left and below is the drop of cervical mucus; to the right and above is the drop of seminal fluid. The spermatozoa have lined up, at the junction of the two drops, with heads directed to the area of mucus.

is to be fertilised, it is essential that the sperms should gain the entrance of the cervix, with its favourable reaction of alkalinity, within an hour at the most, of being deposited in the vagina.

It has often been stated that the occurrence of the orgasm has no influence on conception, and we know that in many cases this is true. But if the orgasm means the outpouring of an alkaline medium by which the sperm is quickly rescued from its stimulating but ultimately fatal acid environment, we can see that the orgasm is likely to favour the subsequent meeting of ovum and sperm.

Further, it has been shown by Séguy, Vimeux and others, that the cervical mucus has other functions than that of modifying the hostile pH of the vagina. They have shown that it has a chemiotactic affinity for the sperm, and also that it provides a medium along which it can travel through the cervix into the uterine cavity.

If a drop of clear cervical mucus be placed on a warm slide alongside a drop of fresh normal seminal fluid, the sperms can

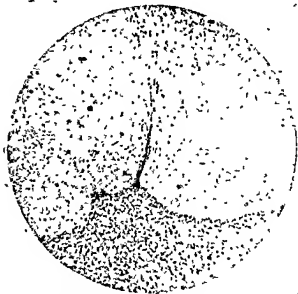


FIG. 43. The sperms are penetrating the drop of mucus in a column, and a second column of invasion is beginning to form.

be watched lining up head first at the border of contact of the two drops (Fig. 42). Very quickly the sperms penetrate the mucus in long columns and later become diffused through the whole drop (Fig. 43). If the vaginal fluid is examined not more than half an hour after coitus, the sperms are found to be dead or dying, except those which have gained the alkaline shelter of the tiny "ilots" of mucus which have not yet become mixed with, and acidified by the vaginal secretion. But in the cervical canal the sperms can be found in large numbers and normally active.

Séguy and Vimeux have shown, however, that the mucus has

not only an alkalisising function, but also that it is necessary as a medium through which the sperm may traverse the canal. They

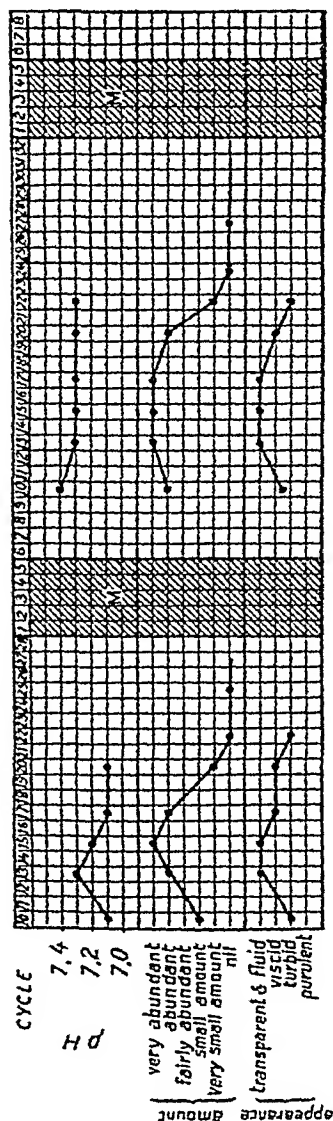


Fig. 44. Graphic variations in the pH, amount, and viscosity of the cervical mucus in a normal woman.

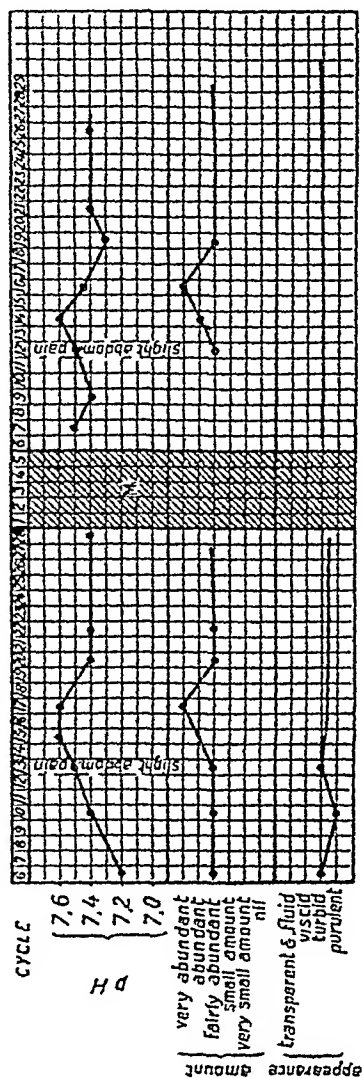


Fig. 45. The maximum activity of the cervix occurs at a later date than in the case of Fig. 38. A slight abdominal pain (? tubal colic) is recorded immediately before the height of secretion, which probably coincides with ovulation.

classify the amount of mucus and its viscosity and quality into different grades which influence the passage of the sperm. The normal conditions are a moderate amount, translucent and thin.

Abnormally, there may be an excessive, viscid secretion, or, on the other hand, a complete absence. In the former case the sperms are strongly attracted to enter the os, but the viscosity impedes their upward progress. An examination of such mucus one hour after shows the sperms to be dying or dead. In the latter case the sperm cannot enter the os or traverse the canal.

A third possibility is a purulent mucus. The medium contains many leucocytes which are found to hinder the activity of the sperms and prevent their passage through the canal.

These details are of remarkable interest, but there is still more to tell.

The production of mucus by the cervix is not the same at all stages of the monthly cycle. Secretory activity rises from the end of menstruation until it reaches its climax from the twelfth

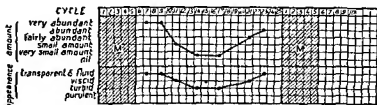


FIG. 40.

to the fourteenth day of the cycle, after which it rapidly diminishes; with the increased secretion, the alkalinity also rises as shown by an increase in the pH (Figs. 44 and 45). The maximum secretion, therefore, coincides with ovulation, a time when the ovum is ready, and the sperm requires the mechanism whereby the two can be brought together. If many women are examined, it is found that while the majority, about four-fifths, produce the maximum secretion between the twelfth and fourteenth day, there are some who have two waves of maximum secretion, one just after the period finishes and the second just before the next period (Fig. 46). Later work will show whether there is any difference between these two types in their capacity for conception, but it is possible that the latter ovulate twice in the month.

Séguy and Simonnet (10) found that in eight of twelve women there was a wave of maximum of cervical secretion which

corresponded with the height of the wave of output of œstrone in the urine, while in two there was no variation in cervical secretion nor in the excretion of œstrone in the urine (Fig 47). A further piece of evidence is that the maximum vaginal desquamation of epithelium which is a constant sign of the period immediately following œstrus in animals, also follows immediately after the maximum secretion of cervical mucus. In women the smear test is not so constant or so sharp as in laboratory animals but Séguy and Simonnet found this evidence in six out of ten women examined.

We find then, that the secretion of chemiotactic mucus from the cervical glands is timed in amount, fluidity and *pH* to coincide with the rupture of the follicle, so adjusted as to render the passage of the sperm as easy as possible. It is almost certainly

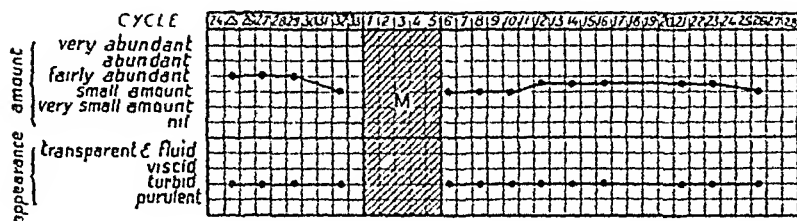


FIG. 47.

controlled by the secretion of œstrogen and largely dependent on it.

### Habitual Abortion

It is true that if a woman can conceive, even though she cannot carry the foetus to full term, she is not strictly sterile, but inasmuch as the net result is that she has no children, she can be broadly classified in the category of sterility. There are some obvious causes of repeated abortion, to which we shall make no reference here, but there are many who have had a series of abortions for which no cause can be found. Our knowledge of the endocrine influence on the genital organs before conception and during pregnancy suggest that these patients suffer from some hormonal abnormality which either kills the foetus or causes a shedding of the decidua and consequent uterine contraction.

The most obvious disturbance is a failure of the corpus luteum. It is responsible in part, if not entirely, for the formation of decidua and growth of the uterus and there is clinical and



Abnormally, there may be an excessive, viscid secretion, or, on the other hand, a complete absence. In the former case the sperms are strongly attracted to enter the os, but the viscosity impedes their upward progress. An examination of such mucus one hour after shows the sperms to be dying or dead. In the latter case the sperm cannot enter the os or traverse the canal.

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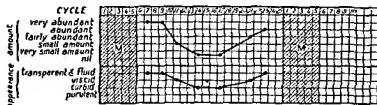


FIG. 46.

to the fourteenth day of the cycle, after which it rapidly diminishes; with the increased secretion, the alkalinity also rises as shown by an increase in the pH (Figs. 44 and 45). The maximum secretion, therefore, coincides with ovulation, a time when the ovum is ready, and the sperm requires the mechanism whereby the two can be brought together. If many women are examined, it is found that while the majority, about four-fifths, produce the maximum secretion between the twelfth and fourteenth day, there are some who have two waves of maximum secretion, one just after the period finishes and the second just before the next period (Fig. 46). Later work will show whether there is any difference between these two types in their capacity for conception, but it is possible that the latter ovulate twice in the month.

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Further light on habitual abortion has been obtained by the discovery of an accessory food factor called vitamin E. It was reported in 1922 and described in 1925 (12 and 13) that rats could not reproduce when fed on certain diets. Their œstrus cycles were unaffected, and they conceived, but they resorbed their foetuses before full term.

In the male, vitamin E privation causes an incurable degeneration of the germinal epithelium of the testis; in the female there is no change in the ovaries or other genital organs, but the foetus dies during pregnancy before viability. The condition is curable, and if the necessary foodstuffs are given during a succeeding pregnancy, the foetus will be delivered normally at full term.

Vitamin E is found in small amounts in animal tissues, less in the viscera than the muscles, and in very small quantities in milk (14). It is altogether absent in the tissues of animals deprived of the vitamin by suitable artificial feeding. It is found in large quantities in the wheat germ, and also in lettuce and other leaves. It is absent in cod-liver oil, which is so rich in vitamins A and D, but is present in vegetable oils, such as cotton-seed oil and olive oil.

While sterility can be prevented by the ingestion of minute quantities of vitamin E it is impossible to influence fertility by increasing the dose. The litters of young rats were not increased in numbers or weight when the pregnant females were fed on doses up to twenty times the minimum dose to ensure fertility. There is evidence of the body's capacity to store the vitamin, for if a single large dose be given at the beginning of pregnancy, it is sufficient to last during the whole of gestation and thus ensure the birth of a normal living litter.

Vitamin E is fat-soluble, but almost insoluble in water. It is remarkably resistant to heat, light and desiccation. Exposure to a temperature for several hours of 180° C. fails to destroy it, and distillation *in vacuo* up to 233° C. has not altered its potency. It is not destroyed by acids and alkalis at ordinary temperatures: in fact it can resist the action of concentrated sulphuric acid and boiling 20% caustic potash.

Whether deprivation of vitamin E can play any important part in causing abortion in woman is doubtful, for it is difficult to imagine a diet in which vitamin E would not have a place. But it is possible that re-inforcement by administering it therapeutically might have a useful effect. We shall refer to the results obtained in the section on treatment.

## TREATMENT

**Defective Ovulation.** In laboratory animals maturation of the follicle can be immensely stimulated by one of the pituitary gonadotropic hormones. If this hormone could be given to women in sufficient doses, it is possible that a similar effect would be produced, but, as yet, there is no certain separation of these hormones or adequate dosage suitable for clinical work.

A means of stimulating the germ elements of the ovary lies in small doses of X-rays. In 1915, Van de Velde showed that such doses would establish menstruation in certain cases of amenorrhœa, and others found the same could be obtained by X-raying the pituitary gland.

The ovarian cells are susceptible to the action of X-rays. Larger doses kill the large follicles, then the small undeveloped follicles, the corpus luteum and, finally, the most resistant tissue, the interstitial cells. But while large doses kill, small doses stimulate, and it is on this fact that is based the treatment of sterility by X-rays.

Edicken (15) reports the following technique and results. The exposures are given twice weekly for three weeks, at intervals of three days, the first over a large field to include both ovaries, and the second over the pituitary by a small field.

The technique is the following dose, 127 kV., 5 MA., 14 in. distance, 5 mm. aluminium filter for three to five minutes: equivalent to  $7\frac{1}{2}$  to  $12\frac{1}{2}$  S.E.D.

The results of treatment for sterility are reported. Number of cases, 33.

Total pregnancies, 15 (in 14 women).

Normal full-term children, 11.

Premature deliveries, 1.

Pregnant, but undelivered, 3.

and the periods of sterility ranged from three to eighteen years.

**The Fallopian Tube.** The obvious rôle which the tube may play in causing sterility is that of obstructing the passage of the ovum. How far spasm and stenosis may operate we do not yet know.

Rubin's insufflation of the tubes which was first introduced twenty years ago as a test of patency has now become, in addition, a treatment for sterility, for a sufficient number of cases of pregnancy have followed the test to prove that, even allowing the coincidence, it can be curative.

In 1932 Rubin (16) reviewed the results of the previous twelve years' experience of tubal insufflation. Many interesting points emerged which do not properly belong to the present chapter, but his results of treatment for sterility may be set forth. The test was satisfactorily applied in 2,192 patients for sterility, and of these 947 (43·2%) had normal patency; a further 1,245 (56·8%) had various degrees of tubal obstruction. Of the total series 26·1% had complete tubal obstruction, and it is these 572 patients who can be fairly claimed to be suffering from tubal sterility, whatsoever other conditions may have co-existed.

Repeated insufflation of the same patient has shown that it is possible to restore or improve tubal patency. Of Rubin's series, 87 cases of peri-tubal adhesions showed either improvement or complete restoration of normal patency after one or more insufflations; similarly, 63 cases of stenosis and 22 of tubal spasm showed improvement. The most striking effect of insufflation, however, was shown by 116 cases, who, on the first occasion, showed complete obstruction, but who subsequently were found to have varying degrees of permeability. There is, therefore, much evidence that obstruction of the lumen can often be overcome by one or more insufflations. The series of tracings afforded by kymograph is invaluable in all cases requiring repeated insufflation.

The curative value is best exemplified by the number of pregnancies which follow quickly after insufflation, performed five years or more after marriage, where some abnormality of the tube was discovered. These conditions are strict enough to test the value of insufflation as a treatment of sterility. Successful results have been reported by many writers, and Rubin's own results are published as follows:—

Normal patency: of 947 cases, 26·82% became pregnant; of 103 cases of tubal spasm, 20·38% became pregnant, and 21·58% of pregnancies followed insufflation that was done for strictured or adherent tubes. And, of all these patients, 27·89% became pregnant within one month of the test. The time after marriage at which treatment is applied is also important. Rubin reports that 22·13% of the successful cases had been married for five years or more, and 44·15% of cases of secondary sterility successfully treated had waited five years or more since their last baby.

The results published by King (7) indicate that, of his whole series of 272 sterile patients, 6% became pregnant, but with 24 tubes were found to be patent, 11·6% subsequently had

**Operations on the Tube.** It would seem that, if the tubes were found closed, and that if repeated insufflations failed to open them, the natural corollary would be an operation to open them by making artificial stomata. This would obviously be contra-indicated if the tubes were grossly diseased. The results of all operations, however, have been disappointing, except those performed for occlusion of the fimbriated ends where the tubes are otherwise normal. Solomons (17) reports the results of 366 operations for blockage at the fimbrial end, isthmal stenosis and obstructions of the interstitial portions. Of the 366 cases pregnancy followed in 8.2%. This is a comparatively small success, which makes us hesitate before recommending a woman to undergo laparotomy.

If, however, we consider only those operations which released the fimbriated extremity from adhesions, the results are good enough to justify operation, provided the diagnosis has been properly established by kymographic insufflation, or if necessary, salpingography after injection of lipiodol. Meaker (18) states that pregnancy followed in 10 women of 19 who had been operated upon, of whom one had an ectopic gestation. Of these limited cases of salpingostomy, Solomons found 32 pregnancies followed 72 operations, of whom 16 became pregnant within one year of operation.

When the isthmus is obstructed as a result of former inflammation, operation is all but useless. If, however, the obstruction takes the form of a U- or S-shaped kink, presumably congenital in most cases, it is possible to excise the obstructing kink and make an end-to-end anastomosis over a thread of No. 1 catgut, which is passed from the ampullary end through the distal and proximal segments into the uterine cavity. The catgut strand is left *in situ* and is later absorbed. Where the technique of the operation has been good subsequent X-ray examination by lipiodol shows a patent tube.

**Failures of Fertilisation.** Under this head, we shall consider those cases in which the sperm, though deposited normally in the vagina, is unable to make the passage of the cervical canal. As we have already shown, the factors favouring conception are suitable pH values of the vagina and a normal amount of translucent fluid mucus in the cervical canal.

It is probable that the acidity of the vagina is never sufficient to kill all the sperms, provided that conditions are such that they are able to gain entrance into the cervical canal within one hour

after deposition. The fault therefore lies in the cervical secretion. There may be either no mucus or a quantity of purulent or too viscid secretion.

Huner's test is the microscopic examination of a platinum loop full of the cervical canal fluid one hour after coitus. In some cases of sterility without any obvious physical signs the sperms removed in this manner are found to be dead. There is, therefore, some hostile element present in the cervical canal which kills the sperms. It may be that the pH of the canal is unfavourable, or some other influence of which we are ignorant.

It seems certain that the secretion of translucent fluid mucus is stimulated by circulating oestrogen, and, though we know of no published results, it would seem that the rational treatment would be the administration of oestrone during the four days before the thirteenth day of the cycle. This is on the assumption that, in a given case, ovulation takes place on the thirteenth or fourteenth days. Strictly, an attempt should be made to determine the date of ovulation by estimation of oestrone in the urine, taking the day of maximum output as coinciding with ovulation. This is a laborious biological estimation, and may, in some patients, show no distinguishing fluctuation. If, however, say 10,000 units of oestrone are given each day from the eleventh to the thirteenth days and from the thirteenth to the fifteenth days in later months, it is probable that sooner or later the date of ovulation would be correctly preceded by the injections. The type of woman here considered is one who never experiences the orgasm, and is ordinarily frigid. The latter is probably of purely psychological origin, and is not always, or often, related to failure of ovulation.

When the cervix is discharging large quantities of turbid or purulent viscid mucus-pus, the obvious treatment is that of the infection. An account of this will be found in the chapter on Leucorrhœa. Even in these cases, however, it is not always easy to find evidence of infection apart from the nature of the discharge. In the majority, a really cleanly applied swab to the cervical canal will fail to grow an organism, and the presence of leucocytes does not necessarily mean pus. Further, microscopic examination of cervices which are confidently labelled "cervicitis" by ordinary clinical examination, often finds it very difficult to establish definite signs of infection. A survey of all the phenomena of the cervix irresistibly suggests that excessive secretion, even if apparently purulent, is by no means always due to infection or

the results of infection, and just as deficient secretion is due to hormonal influences, so may excessive discharge be due to the same general cause. In the latter case, the logical treatment should be, therefore, to give the opposing hormone (progesterone) during the days immediately before the assumed date of ovulation.

**Artificial Insemination.** Hitherto, this method has not gained much favour in clinical medicine. It consists essentially in passing the sperms beyond the vagina and cervical canal directly into the uterine cavity. It should therefore be reserved for those cases which we have just described, where the fault lies in the inability of the sperms to traverse the cervical canal by reason of either insufficient or excessive abnormal secretion.

In view of the necessity for correlating insemination with the date of ovulation, it can only be successful if it is properly timed during the monthly cycle for two days before ovulation is expected to occur. Séguy and Simonnet report several successes when the timing was adjusted to the day of maximum output of cervical mucus, and they describe some successful results where there had been failures when the proper timing had been neglected.

The evidence is, therefore, that where ovulation occurs normally and the tubes are patent, insemination has a real chance of success, provided it can be performed immediately before rupture of the follicle.

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## CHAPTER X

### LEUCORRHOEA

**Definition.** Leucorrhœa may be broadly defined as a functional excess of the normal secretions of the cervix and vagina, or the existence of a white discharge containing pus and other abnormal elements due to an infection. While it is a simple matter to make a diagnosis of leucorrhœa by clinical or bacteriological examination, it is not always easy to estimate the amount by the ordinary questions of case-taking. Women's ideas vary considerably on what is normal. What to one may be of no importance may to another be sufficient for her to demand treatment. Some women seem to care little about a leucorrhœa which is enough to mark clothes, but others will be anxious and distressed out of all proportion to the seriousness or even inconvenience of the condition.

It is, therefore, necessary to regard the disease objectively and form one's own estimate of the amount or even the existence of a discharge by clinical and microscopical examinations. The same remark applies to assessing the result of treatment. A true idea can only be formed by examination, and not by questions alone. Leucorrhœa is of considerable importance, firstly because it is a very common condition, secondly because it is liable to cause much distress of mind, apart from local inconvenience, and thirdly it is often difficult to cure.

Further, it may be added that the study of excessive vaginal discharges has added, and will add still more, to our knowledge of the physiology of the pelvic organs.

#### Vaginal Flora

The study of the bacteriology of the vagina began with the work of Döderlein in 1892, who first described the existence of a Gram-positive bacillus, which he stated produced lactic acid in the vagina.

This organism, now known as Döderlein's bacillus or *B. vaginalis* is a member of the lactobacillus group, and is closely associated with *B. acidophilus* and *B. bifidus*. Very much work has been done (see bibliography) on the cultural and morphological characters of this organism in an attempt to find its place in the acidophilus group, but owing to the pleomorphism, both of



the microbes and their colonies on different media and by different subcultures, it is a very difficult problem, either to identify it with one or other defined members, or to establish it as an entirely separate individual. The fermentation tests are not sharply demarcated. Acid production in some sugars may require as much as seven days, while in others the reaction is only partial. Thus they are difficult to differentiate from reactions produced by related organisms.

It has been noted (Brown and Redowitz), however, that Döderlein's bacillus is serologically different from acidophilus, but they also found that different strains of apparently the same organism, as obtained from different normal women, did not agglutinate each other.

All workers are agreed that the organism belongs to the aciduric group, and that it is probably a separate individual. It is ill-defined, however, and may have developed its special characters by the peculiar cultural conditions of its habitat.

Its derivation is also not known, though it is probable that in the new-born infant it comes from the intestine, and becomes modified by the pabulum of the vagina.

It has been shown by Cruikshank and Sharman that, while the vagina at birth is sterile, it becomes infected by the *B. vaginalis* about the third day. Cultures prove its presence until about the tenth day, after which it disappears in the majority of children (75%) until puberty. From puberty to the menopause it can generally be recovered from healthy women. After the menopause it disappears.

This general statement is not entirely true. Some authors (Weinstein and others) found that before puberty about 17% of children harboured Döderlein's bacillus, and that, of ninety-nine non-gravid adults, thirty-eight had the bacillus. Of ninety-seven pregnant women, the microbe was found in 88%. These figures are rather lower than those of some other workers. Where there is specific infection, either of gonococcus or trichomonas, Döderlein's bacillus is not found. We may, in general, say that the bacillus is not found in association with cases of pyogenic or, indeed, any pathological infection. We shall reserve for a later section a discussion on its protective power against vaginal infection.

While the vaginal bacillus is the most important and constant feature of the vaginal flora, yet other non-pathogenic organisms are frequently found. One or other variety of the diphtheroid

group is common. They usually grow in very small pin-point colonies, and less commonly as smooth creamy colonies up to 4 mm. in diameter. Pettit and Hitchcock found of sixty cultures from normal pre-pubertal vaginae, forty-eight grew a diphtheroid organism. They are probably of no importance, and exist purely as saprophytes. From a large number of adults also, diphtheroid colonies can be grown. In normal health Gram-positive cocci and Gram-negative bacilli are seldom grown in any but an occasional colony, though they may be seen in a smear preparation.

The highly acid reaction of the normal vagina ( $pH$  4 to 5) probably prevents active growth of coccal organisms, but where Döderlein's bacillus is absent, as before puberty, and after the menopause, a coccal flora can very quickly be established.

In inflammatory conditions the general appearance of both culture and smear of vaginal discharge is entirely different. A pure growth is seldom found. The smear preparation shows a vast number of microbes, chiefly coccal forms, and usually complete absence of the Gram-positive acidophilic bacillus. It is impossible by examination of a smear preparation to be sure of the organism chiefly responsible for inflammation, but by culture it is often obvious, as we shall show later, that one or other colony is pathogenic.

Swabs from the normal cervix are nearly always sterile. There may be an occasional contaminating colony derived from contact with the external os, but if great care is taken it is seldom that a colony can be grown or an organism seen in the smear made of the clear water-white mucus.

In pathological conditions it is possible to find microbes in the smear, such as streptococci or gonococci. But despite the slightly alkaline  $pH$  of the cervical mucus it is normally sterile.

### The Acid Reaction of the Vagina

Between puberty and the menopause the vaginal secretion is acid, unless an infection is present. The reaction varies between  $pH$  of 4.0 to about 5.5, and is usually about 4.5. It varies slightly at different times of the monthly cycle, tending to be more acid during the "oestral" fortnight following menstruation than in the "luteal" preceding the next menstruation. It is due to the presence of lactic acid in a concentration of about 0.75%. The method of production of lactic acid has been strongly debated. It is agreed that it is derived from the glycogen of the vaginal epithelium, just as it is a precursor of lactic acid in other parts

of the body, the muscles for example ; and there is a rough parallel between the amount of glycogen in the epithelial cells and the degree of acidity of the vagina.

In favour of the existence of a ferment action are Kleinlein (1926), who found lactic acid in the vagina of the new-born before bacterial invasion had occurred, and Blair Bell, who found lactic acid in sterile hæmatocolpos fluid. Shroeder states that *in vitro* Doderlein's bacillus cannot attack glycogen, and Smorodinzen states that if the glycogen of "*in vitro*" experiments is chemically estimated there is no evidence of glycogenolysis by *B. Doderlein*.

On the other hand, Bourne and Frazer, after a most careful examination of hæmatocolpos fluid (pH 7.88), could find no trace of lactic acid or any reducing substance. The evidence is conflicting, and there is still no certain knowledge of the problem. The writer feels that, whatever may be the possibility of enzymal production of lactic acid, in normal adult life the chief agent is the acidophilic vaginal bacillus.

The importance of the acid reaction of the vagina lies in its antiseptic power against most pathogenic organisms. Before puberty and after the menopause, when the pH is usually around the neutral point, or definitely alkaline, septic infections are common, but a true vaginitis (apart from gonorrhœa and trichomoniasis) is seldom seen during the child-bearing age. Further, laboratory experiments on associated culture of the vaginal bacillus and pyogenic cocci show that the latter cannot grow in a medium in which *B. acidophilus* is well developed. Cruikshank reports an experiment in which Gram-positive cocci, diphtheroids and Doderlein's bacillus were inoculated into glycogen-serum-broth. For the first three days subcultures showed staphylococci to be the predominant organisms. On the fourth and fifth days the pH of the culture tubes fell from pH 6 to 5.6, and only *B. Döderlein* and yeasts could be found on subculture. In the control tubes there was no evidence in smear or culture of lactobacilli. Clinical evidence which supports the laboratory experiments is also forthcoming. For example, from normal women no growth of cocci or contaminating organisms can be obtained after coitus or the use of douche nozzles.

While it is generally true that pathogenic organisms cannot easily grow in the normal acid vagina, yet the group of faecal streptococci (or enterococci) are able to grow in a medium of pH 4 to 5, and are therefore able to produce a mild vaginitis. Infection by the trichomonas is also possible in the acid vagina. Gonococcal

infection is more difficult to understand. If the organism were deposited only in the vagina it would be impossible for it to survive, but it is probable that, while still surrounded by an alkaline semen, it is taken up into the cervix, where it finds an alkaline medium exactly suiting its biological requirements.

The highly acid vagina immediately before labour is a strong natural protection, but after delivery the vaginal reaction is altered by the profuse alkaline lochia, so that any infection contracted during labour has no difficulty in surviving in the favourable lochial medium.

It seems, therefore, that against the risk of ordinary pyogenic infection the acid reaction of the vagina is a sufficient defence, but this resistance is either absent or inadequate in certain circumstances, for example, against certain enterococci, the gonococcus when deposited into the cervical canal, and the trichomonas.

### Clinical Varieties of Leucorrhœa

Certain cases of leucorrhœa may be classified according to age incidence. For example, vulvo-vaginitis of children and post-menopausal infections are chiefly septic and due to invasion by pyogenic cocci. In about a quarter of the children the infection is said to be primarily gonococcal, but soon after the initial infection, a pyogenic infection is predominant. During the child-bearing period of life vaginitis is uncommon, but there is a specific form of vaginitis due to the trichomonas vaginalis. This organism is a triflagellate protozoon about  $16\mu$  long. It is associated with a purulent discharge containing small gas bubbles due to a gas-forming organism. The discharge causes irritation and soreness, and is very difficult to treat successfully. A pyogenic infection, such as enterococcus, is always associated with the trichomonas, and is believed by many to be the real cause of the inflammation. The discharge is always acid (pH 5 to 6).

After excluding the comparatively uncommon cases of true vaginitis we find the great majority of cases of leucorrhœa are due to an excessive secretion of cervical mucus (trachelorrhœa). This is the basic feature of almost all leucorrhœa. The cervix normally secretes enough mucus to maintain the vagina moist, but when, under certain conditions, the amount of mucus is so increased as to be noticeable by the patient, she is said to have leucorrhœa. These conditions may be caused by the secondary infection subsequent to gonorrhœa. Deep tearing of the cervix by child-bearing, and

increase of the gland-bearing area by eversion, ectropion or erosion predispose to its occurrence. In addition to these definite organic conditions, there is functional cervical activity, showing itself by excessive secretion of mucus in the absence of any form of infection and without any naked-eye or microscopic change being obvious. This condition is typically seen in virgins and can be termed "non-infective vaginal leucorrhœa."

There are other varieties of leucorrhœa; discharges may be found as the result of new growths, ulcers and other organic states, the treatment of which is obvious.

### Investigation of a Case of Leucorrhœa

It will be convenient to consider this section under age periods. **Children.** Nearly all cases show a mild redness of the labia. *and intense redness of the hymen and lower part of the vagina.* There is a small amount of sero-purulent discharge. The chief point for investigation is the presence of the gonococcus. Examination for this infection should be made in the usual way by smear preparation, culture, and complement fixation test. A negative finding is of little value as excluding the infection. A fresh specimen should be examined for the presence of trichomonas. The child should also be examined for thread-worms and parasites. The irritation of the anus causes scratching which may infect the peri-anal area and vulval mucous membrane.

**Adults of Child-Bearing Age.** The woman should be examined on a day when she has not used a douche, by speculum, to note first, whether the amount of discharge in the vault of the vagina corresponds with the patient's description. It may be white or mucoid, or a combination of both. A sample is taken from the vault on a swab for immediate culture on blood-agar and simple agar. Two smears are made on glass slides, and a second sample is taken either on another swab, or in a pipette for testing the pH by the universal indicator. The reaction of the vagina is an important factor, and a knowledge of the pH is useful in helping us to know the cause of the discharge. For example, if the reaction is strongly acid (pH 4 to 5) we know that the vaginal flora will be acidophilic (grade I) in which a pyogenic flora cannot live. The material may have the appearance of pus, but it is unlikely that many leucocytes will be seen and the turbidity is due to large numbers of exfoliated vaginal squames. If, however, the pH is 6.0 or over, the normal acidophilic growth will be very small or absent, and the main feature will be a growth of Gram-positive

cocci. When the pH is 7.0 or above, the infection is frankly septic and nearly always associated with vaginitis. If the material is fluid or copious a loopful should be taken for examination of the fresh drop, in order to search for *trichomonas vaginalis*.

After the discharge itself has been examined and removed by a swab, the vaginal wall is examined. It may be uniformly red, rather "shiny," and with feebly developed rugæ. This condition of the vaginal wall is often associated with a fluid discharge, a moderately acid reaction, and *trichomonas* infection. A common form is a general redness, with multiple deep red spots, especially in the vault around the cervix. Punctate vaginitis is chiefly found after the menopause, but quite often before it, and is associated with a purulent discharge, an alkaline or feebly acid reaction, and a pyogenic infection. A third condition of the vagina, characteristic of the young nullipara, but again not limited to this age-group, is a pale mucous membrane, thick and strongly rugose. Microscopic sections will show a very thick squamous epithelium and a high glycogen content, not only of the superficial cells but also of the Malpighian layer. This appearance is characteristic of the œstral period, and is often associated with a profuse discharge of clear cervical mucus, free desquamation of epithelial cells, and a strongly acid reaction (pH down to about 4.0). These patients have no infection. The smear shows no pus cells or Gram-positive cocci, but a large number of Gram-positive rod-shaped bacilli (*Döderlein's bacillus*). The culture from these cases also grows nothing but acidophilic bacilli.

In many other cases a careful inspection of the vaginal wall will reveal nothing abnormal. Here again there may be no true infection which can be demonstrated by smear or culture.

After the vagina has been examined the condition of the cervix is noted. When the cervix has been exposed by a speculum the external os is carefully cleaned, and very carefully a sterile swab is passed into the canal and turned about to obtain a specimen of the secretion. A smear and culture should be made as for the examination of the vagina. It has been the custom to attribute all changes in the cervix, apart from new growth, to infection and inflammation, but we are gradually realising that many conditions, hitherto regarded without question as inflammatory, are now to be attributed to the prolonged action of an excessive production of oestrogen. Though this hypothesis is not yet proved, we have accumulated evidence in women, and evidence of cervical changes

in monkeys after prolonged treatment by œstrone (1) (2), which indicate that the cervix as well as the vagina and uterus undergo cyclic changes under the influence of the ovarian hormones. All examinations both of the cervical secretion and also of histological sections will often fail to show the slightest sign of infection or inflammation. It is an important clinical point to ascertain if the symptom of leucorrhœa is due to infection or disturbance of hormone production, for obviously the treatment must be entirely different.

The acute stage of an infective leucorrhœa presents no difficulty. There is an angry red rim around the external os, through which exudes a drop of viscid yellow pus. Cultures on suitable media will grow gonococcus or other pathogenic organism of which streptococcus progenes is the chief.

### Chronic Cervicitis

The chronic form of cervical infection presents a different problem of diagnosis. It is generally assumed that if there is leucorrhœa associated with a lacerated and everted cervix the condition is one of chronic cervical infection called chronic cervicitis. It is important to be clear on this question of chronic cervicitis because if it is actually present, maintained in activity by a continuing infection, then it exists as a chronic septic focus, liable to produce a low-grade toxæmia and local conditions such as peri-lymphatic fibrosis, which, in their turn may cause pelvic pain and backache. If, however, the leucorrhœa is no more than an excess of mucus (and squamous material) derived from glands hypertrophied under the influence of a long past infection, but not now containing organisms, then the symptoms often ascribed to "chronic cervicitis" cannot be explained on this hypothesis. The result of cervicitis is certainly leucorrhœa; but can infection, apart from gonorrhœa, persist indefinitely in the cervix as a live active focus causing toxæmia, pain and backache? The question can be answered by the results of searching for evidence of infection in these long-standing cases of lacerated cervix with leucorrhœa. The following are the findings:—

1. The secretion taken from inside the cervical canal is almost always sterile by any form of culture. The smear shows scarcely any cellular elements and usually no organisms. The mucus is clear and translucent. These remarks do not always apply to post-

gonorrhœal infection, but even in these cases it is not uncommon to find no signs of any form of infection.

2. Histology of the cervix shows hypertrophied and actively secreting glands but never can organisms be seen within the glands and almost never is there any cellular infiltration around the glands. So called "catarrh" of the glandular epithelium described by some investigators is indefinite and unconvincing as evidence of continued infection of the cervix. The glands may contain some cellular *débris* but pus cannot be seen within them. Fibrosis of the submucous tissues may be demonstrated but even this evidence of chronic inflammation is not always present.

3. Séctions stained by Twort or Giemsa methods have never, in our experience, demonstrated microbes in the glands or tissues, though if artificially injected or massaged into the tissues they can easily be seen.

4. Cultivation of cervical tissue, properly cauterised to obviate contamination, in both aerobic and anaerobic broth for many days do not yield a pathogenic growth.

5. Cultures of the mucus from Naboth's follicles are usually sterile. In one or two cases a few colonies of coliform bacilli have been grown (Bourne and Bond, 4).

Careful search for live infection in so-called chronic cervicitis has, in our hands, failed to find evidence of its existence.

Where there is an erosion it is true that the reaction of inflammation is found patchily distributed in a very thin layer beneath the surface where the squamous epithelium has broken down. The degree of reaction in many cases is, however, so mild and superficial that it is probably due to the irritation of the acid vaginal secretion and not an expression of a true infection of the cervix. Small polypoid pieces of the cervical mucosa not only on an erosion but within the cervical canal are crowded with leucocytes and there are many polymorphs within the capillaries of the polypi, but these appearances are found in perfectly normal cervixes.

We believe, therefore, that the majority of cases commonly called "chronic cervicitis" are not examples of true inflammation. They are cases of old injury at labour with possibly a transient low-grade infection at the time which quickly disappears, followed by hypertrophy, and excessive secretion arising from greatly enlarged glands. But in a small number infection may still be found in "chronic cervicitis" and it is well always to take a culture from the canal.



Figs. 48 to 51 are taken from low-power magnification (7 diameters) of the cervical canal prepared by Dr. L. T. Bond. They indicate conditions of the glands in normal cases, hypertrophy, and "virginal erosion."

Fig. 48 shows the development of the glands in a multiparous woman, aged thirty-nine, whose uterus was removed for fibroids. There was no leucorrhœa, but the half shading at the squamo-

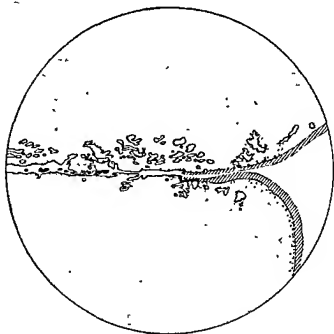


FIG. 48.

columnar junction and also of the minute polypoid bodies in the canal indicates a round cell infiltration which amounts to "chronic inflammation." The epithelial junctions and intra-canalicular polypi show these round cell infiltrations in nearly all cases examined. It is doubtful therefore whether they should be regarded as indications of true inflammation.

Fig. 49 is a cross section of the cervical canal of the same patient, and shows a normal glandular arrangement and no sign of any form of histological inflammation.



FIG 40.

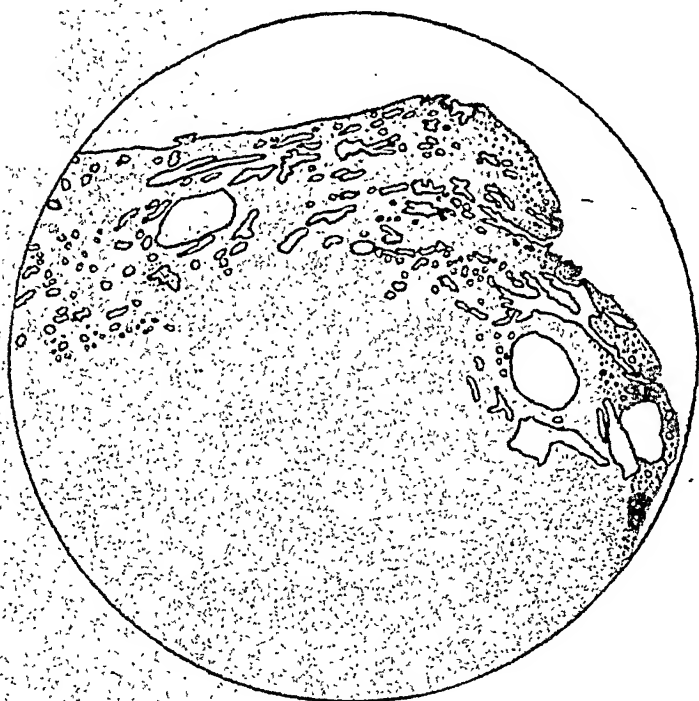


FIG. 50.

Figs. 50 and 51 represent the cervix of a parous woman, aged forty-seven, having "chronic cervicitis" and profuse leucorrhoea. Fig. 50 shows the end of the canal and the portio vaginalis

which carries an erosion. Sub-acute or chronic inflammation is seen superficially beneath the erosion (as shown by areas and spots of half shading), extension of the glands beneath the surface of the erosion on the portio vaginalis, cystic distension, and great hypertrophy of the glands, but only in one deep gland is there any round cell exudate suggesting that the glands contain an inflammatory irritant.

Fig. 51 is a section of the canal of the same patient. Again

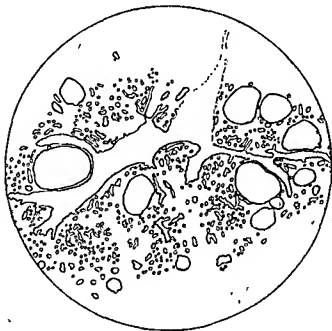


FIG. 51.

there is enormous hypertrophy and deep downgrowth of the glands with many cystic dilatations, but no histological evidence of infection.

Bond (4) in his description of these sections says: "These pictures make it difficult to believe that infection can be present deep in the glands of the canal, since, were pathogenic organisms there, they must surely give some evidence of their presence in the shape of an inflammatory reaction in the adjacent tissues; on the other hand, the very superficial distribution of that inflam-



FIG. 52.

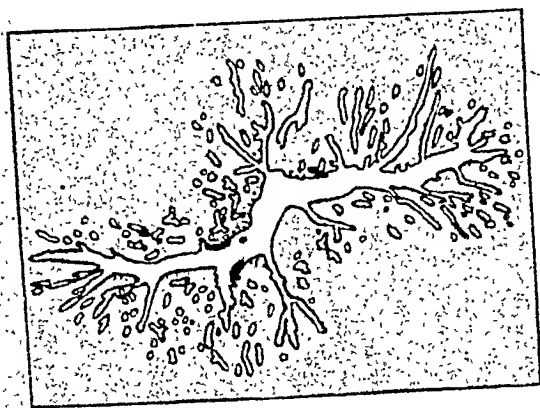


FIG. 53.

tion which is present, *i.e.*, in the erosion, cannot but suggest that its cause originates on the surface, and not from the fundi of the glands, and that the irritant must exist in the vagina since it appears not to be effective within the canal."

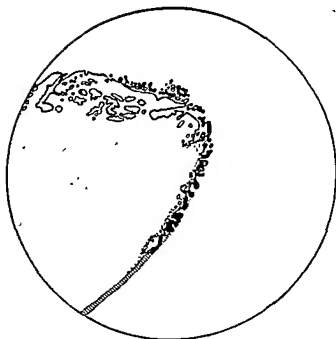






FIG. 54.

-  = Fibro-muscular tissue of cervix.  
 = Chronic inflammation.  
 = Acute inflammation.  
 = Squamous epithelium

Key to shading of diagrams of sections of cervix  $\times 5.25$  diam. (Bond.)

Figs. 52 and 53 are taken from a parous woman aged forty-two, who had an operation for prolapse, but complained of only slight discharge. The cervix was lacerated and the lips were everted. Fig. 52 is a section taken at the external os at the junction of the squamous and columnar epithelia. There is extension of glands beneath normal squamous epithelium on one lip and loss of the

squamosa on the other lip. There is also a mild and superficial inflammation but only in one or two places around the glands. The transverse section shows a normal or nearly normal glandular development for a parous woman of forty-two, and only in two small areas is there a mild exudate of chronic inflammatory cells.

Fig. 54 shows a section from a "non-infective vaginal erosion," of a *virgo intacta* of twenty-two. There was an excessive thick mucoid leucorrhœa of *pH* 3.5. The culture grew Döderlein's bacillus and some anaerobic diphtheroids. The cervix carried a bright-red circular granular erosion.

There is no glandular undergrowth beneath the squamosa as in the other examples, but an acute inflammatory exudate into granulation tissue where the squamous epithelium normally should exist. In this case no pathogenic organism could be grown but the vaginal fluid was strongly acid and the inflammatory reaction entirely superficial.

### Bacteriological Examination

Smears from the vagina will fall into one of three categories. Grade I shows large numbers of epithelial cells and Gram-positive acidophilic bacilli. Here and there an occasional leucocyte. Grade III. smear shows large numbers of pus cells and enormous masses of cocci, both Gram-positive and -negative, and few, if any, epithelial squames. Grade II. is a mixture of both grades I. and III. There are occasional bacilli of the acidophilic type and epithelial squames, but also pyogenic cocci and leucocytes. In grade I. the *pH* is strongly acid, grade II. is mildly acid, *pH* 5.5 to 6.5, while grade III. has a *pH* of 6.5 to 7.5.

In cases classed as grade I. there is no infection. Even though there may be quite a profuse discharge, it is not due to active or present infection or inflammation. Grade III. is a true pyogenic infection. associated with vaginitis and commonly seen after the menopause, in trichomoniasis, or in subacute gonorrhœa. Grade II. indicates a mild, low-grade infection, probably by a faecal streptococcus.

The results of the cultures are fairly constant, according to the grades, though it does not follow that the microbes seen on the smears will necessarily be found as colonies on the agar plate, nor that some of the growth on agar will have been seen in the smear. The culture from a grade I. vagina will grow little if anything but colonies of acidophilus (Döderlein's bacillus) with

a varying number of minute colonies of diphtheroids. For a full description of the cultural characteristics of Doderlein's bacillus, we must refer the reader to the bacteriological authors.

The cultures derived from grade III. discharge will consist of colonies of several varieties of cocci, some hæmolytic, both Gram-positive and negative, and some bacilli. Cultures from grade II. again will show a mixture of the features of both grades I. and II. It is always difficult to decide which is the pathogenic organism, but it is probable that any predominant colony on the blood plate—commonly a short-chained non-hæmolytic streptococcus—is of importance. It is very uncommon to find a true hæmolytic streptococcus in a vaginal discharge.

When the cervical cultures are examined we are generally surprised to find the small bacteriological evidence of infection. They are frequently sterile or show an occasional contaminating colony. But if a definite growth is found, usually streptococcal, it is probably the infective organism responsible for the inflammation. The smear will usually show nothing at all except streaks of mucus entangling a few epithelial cells and leucocytes. Sometimes no organisms can be found and seldom more than a few occasional cocci or bacilli which are obviously vaginal contaminants.

Vaginal and cervical cultures are of considerable bacteriological interest, because of the diversity of growth and the frequent surprise caused by inspection of the plates. No real understanding of leucorrhœa can be gained without the detailed examination of many cases, and every gynæcologist should have a certain knowledge of vaginal bacteriology to enable him to appraise the value of the reports which are sent to him.

### Treatment

The treatment of leucorrhœa has made much progress during recent years, since it has been liberated from the conventional idea that painting the cervical canal with antiseptics could destroy organisms in the glands. Let us consider it again under the headings of age-groups.

**Vulvo-Vaginitis of Children.** In addition to local instillation into the vagina through a small rubber catheter, of glycerine and flavine, the child should receive injections of œstrone of about 10,000 units or less, according to weight, twice weekly for two or three weeks. The effect of œstrone is to cause a deposit of glycogen in the vaginal epithelium which, in its turn, induces a growth of

the acidophilus bacillus, and also thickens the vaginal epithelium and so renders it more resistant to infection.

**Senile Vaginitis.** After the menopause the vagina is thin and atrophied, the protective Döderlein's bacillus can no longer be found, and the reaction is neutral or even alkaline. In these circumstances it is not surprising that the vagina can easily become an incubating chamber for pyogenic cocci.

If œstrone in doses of 50,000 units is given to these patients two or three times a week, a remarkable change is quickly produced. The epithelium becomes thicker, more resistant and "glycogenised." The reaction becomes acid and the infection quickly subsides. It will assist the progress of recovery if a saline douche is used twice a day, but no strong antiseptics are required, and local treatment is scarcely necessary. Only in the worst cases, where there is much redness and soreness with profuse thick pus and bleeding, is it advisable to pack the vagina with gauze and glycerine. There is frequently a small uterine hæmorrhage about a week after the last injection of œstrone.

**Non-infective Leucorrhœa of Virgins.** In the majority of cases the condition is trivial, and associated with depressed general health. In a few, however, the discharge is profuse and sufficient to cause some distress. Local examination or treatment is seldom required, but should it be necessary an anæsthetic must be given. The cervix contains a viscid drop of egg-white mucus, and if the portio vaginalis is squeezed with a pair of ring forceps, as much as a drachm of clear mucus can be made to exude from the os. There may be a "congenital erosion," and the internal os is easily dilatable, up to No. 6 Hegar. This is probably a sign of the effect of "hyperœstrinisation" of the uterus which, we claim, is the cause of the mucous secretion.

The vagina is highly acid, pale pink, rugose and has a very thick mucosa. The epithelium is thick and desquamating and contains a large amount of glycogen.

Many of these patients admit that they are only troubled by leucorrhœa either in the middle of the month or just before the period. For the mild cases no treatment is required beyond rest and change, but some young women may be troubled by such a profuse and constant discharge that local treatment is necessary. On the theory that the excess of mucus is due to the action on the cervical glands of an abnormal circulation of œstrone, treatment should be such as would antagonise its effect, and not directed to the local condition. The latter method is an attempt to deal with the



end result, and does not grapple with the underlying cause, but in practice we find that injections of extracts of corpus luteum which might properly be expected to have the desired effect are disappointing. It may be that the dosage commonly used is insufficient, but probably the cause is not only the simple matter of excess of  $\alpha$ strone which we have suggested above.

If, therefore, we are at present unable to ensure a cure by gland therapy, we must use the more empirical method of destroying the cervical glands which are excessively active.

There are two simple methods of direct treatment of the cervix. The first is by electric cautery of the whole length of the canal by the red-hot electrode. Under an anæsthetic the cervix is dilated to about No. 4 or 5 Hegar, and the mucosa is then burnt until it is white and bloodless by the hot electrode. At first there is a free discharge of blood-stained mucus which soon boils. The boiling secretion serves to distribute an even heat over the surface of the canal and necrose the superficial layer. Continued heat soon boils away the mucus and leaves the canal smooth and white. If an erosion is present, it should also be destroyed by deep cauterisation. There is little danger of destroying the mucosa too deeply and thus preventing the reformation of cervical glands. The fundi of the glands penetrate so deeply into the matrix of fibrous tissue that it is not easy to destroy all the glands. The remains which escape the burning effect of the cautery serve to renew a modified glandular epithelium during the following six weeks. Total destruction of the whole mucosa would not be followed by stricture, for the whole raw area of the canal is rapidly lined by a new epithelium derived from the isthmus above and the portio vaginalis below, but it is serious from another point of view, inasmuch as the complete absence of mucous secretion on the cervix almost certainly prevents conception by depriving the sperm of a means of entering the canal and passing into the body of the uterus. At the same time we cannot agree that partial destruction of the mucosa by linear cautery of the length of the canal, causing parallel strips of necrosis, is sufficient. The difficulty is to destroy enough of the glands to ensure the cure of the discharge, and we think this can only be done by burning the whole surface.

There are two dangerous sequelæ of the electric cautery. The first is hæmorrhage, which can be very sudden and serious, about the tenth day, at the time of the separation of the slough, and the second is pelvic cellulitis, which first appears at the end of the

second week. It will cause all the usual physical signs and a febrile illness which may last for weeks.

It was to overcome these dangers and the use of electrical apparatus that one of us devised the method of chemical cautery. Zinc chloride is a salt of great corroding power, rapid in its action and capable of considerable penetration of tissue. The reader must be referred to the original description for a detailed account of the method and for the experimental data on which it is based, but we will give here a brief *résumé* of the more practical points.

The applicator by which the zinc chloride is introduced into the cervix is a stick of porous clay (Allen & Hanbury) 1 in. long and of four diameters, varying from  $\frac{1}{8}$  to  $\frac{1}{3}$  in. A clay stick of suitable size for the cervical canal is placed in a saturated solution of zinc chloride for about twenty minutes. This is long enough for the clay to absorb the solution to its full capacity.

A stout strand of silk-worm gut or fuse wire is passed through the hole in the heel of the stick. The largest size that can be pressed into the whole length of the cervix is chosen, and either with or without an anæsthetic, depending on the tolerance of the patient, the stick is pressed firmly into the cervix until the heel is flush with or even just inside the external os. Care should be taken that the solution does not drip on to the vagina, or a serious burn may follow. The vault of the vagina is then lightly packed with gauze. The gauze and stick are removed in three hours by pulling on the strand of silk-worm gut, and the patient may get up and walk away. The first effect of the zinc chloride is an immediate thrombosis to a depth of about 2 mm. as the salt is absorbed by the tissue. Necrosis of the penetrated tissue is immediate. This can be realised by microscopic examination of the separated slough which shows perfect preservation of the cells and their nuclei.

For the first three or four days all discharge ceases entirely, after which a slight serous exudate appears with a little blood-staining about the eighth day, indicating the separation of the slough. This may be discharged as one greenish piece about the size of the distal part of the little finger, tunnelled by a cavity which was the cervical canal. After the slough has been passed, a sero-purulent discharge is maintained for a few weeks, gradually getting less until it finally disappears about the sixth or eighth week.

Microscopic examination at the end of three mo

complete columnar epithelisation and a few glands which appear to be entirely normal.

It is important to select the right type of case for this treatment. The cervix must not be torn so that the external os or canal cannot grip the stick tightly. If the stick lies wholly gripped by the canal the result is usually satisfactory, but if there is a deep tear which, by eversion of the lips prevents close contact with the stick, a large portion of the canal will be untouched, and the result will be only partially successful.

We have seen no case of hæmorrhage or cellulitis follow the use of zinc chloride, and for properly chosen cases it is a simple, safe and satisfactory method of treating severe cervical leucorrhœa.

**The Leucorrhœa of Parous Women.** Both the electric cautery and zinc chloride may be used for these cases, provided there is no deep tearing of the cervix.

Where by lacerations, eversion and ectropion the cervix has become distorted and deformed, it must either be amputated or repaired. In most cases amputation is to be preferred, but if no secondary fibrotic changes have occurred and no abnormality but simple laceration exists, repair by the operation of trachelorrhaphy may be performed.

Other methods of treatment which have been used in some clinics are diathermy and zinc ionisation. Neither is particularly satisfactory, but some gynæcologists still employ them. They are based on the idea that the cervix discharges abnormally because it is still infected. Except in subacute cases of gonorrhœa this hypothesis is quite wrong. The cervix discharges either because it is under the influence of an endocrine stimulus or because secondary changes leading to great hypertrophy of the glands have taken place. In both cases the only hope of cure is by destruction of the glands and not by destruction of an infection which in so many patients no longer exists.

### Trichomoniasis

*Trichomonas vaginalis* is a flagellate protozoon, a little larger than a leucocyte, of elliptical shape with pointed extremities. There are three or four flagellæ at the head, and a long style projecting from the caudal end (Fig. 55). It can be seen in a fresh specimen of the discharge diluted with normal saline and placed on a warm microscope slide. It is essential that the examination should be made within a few minutes of removing

the drop from the vagina, i.e., before it has had time to cool.

The organism is recognised from other cellular elements of the drop by its motility. The flagellæ can be seen lashing the

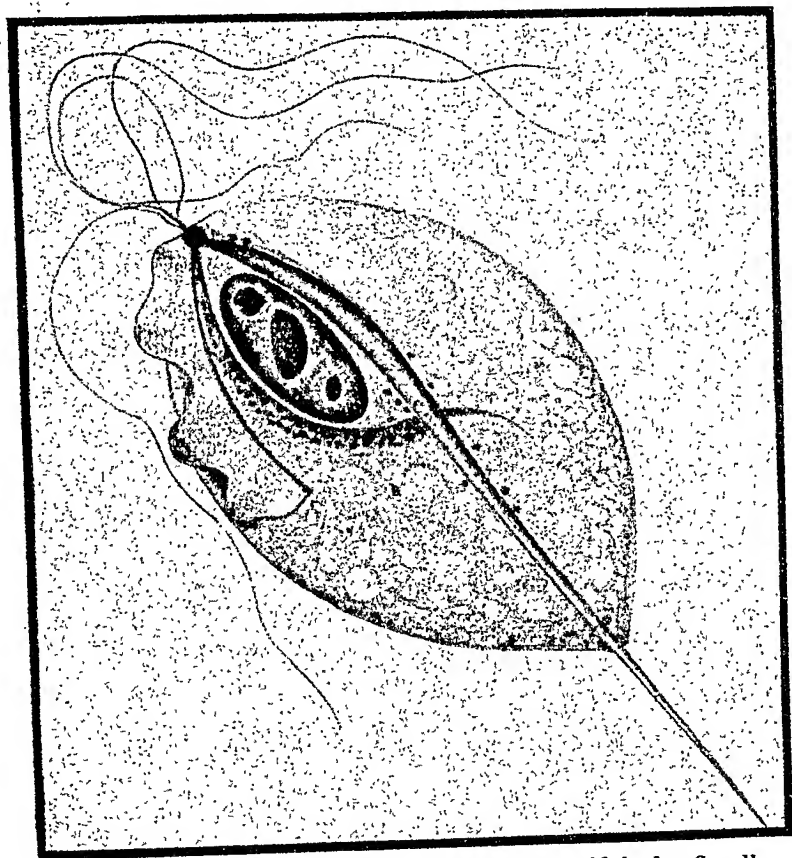


FIG. 55. *Trichomonas vaginalis*. Note the ovoid body, flagellæ, undulating membrane, stoma, and long axostyle. (By permission of Messrs. John Wyeth.)

fluid medium and setting up movement of neighbouring pus cells (Fig. 56).

The symptoms are malodorous purulent discharge, which, if not treated is constant and persistent. It is yellowish or yellow-pink and often contains fine bubbles. There is local soreness, sometimes pruritus and tenderness of the vagina. On passing a speculum the vagina is uniformly red, smooth and liable to ooze

points of blood on swabbing with dry cotton wool. It can infect females of all ages from early childhood to after the menopause, and it is particularly common during pregnancy.

A severe case of *trichomonas leucorrhœa* often causes much distress and depression and even symptoms of ill health. Its origin is not known but it may be derived from the intestine or



FIG. 56 Specimen of vaginal pus containing *trichomonas vaginalis* shown by dark ground illumination. The field also contains a few pus cells, a few epithelial cells, and numerous bacteria.

by indirect contact with other infected persons. It may be transferred from the male during coitus.

The film preparation shows a large number of pus cells, some individual red cells, a few vaginal squames, an enormous number of cocci and bacilli, which include the enterococcus and coliform microbes, and a varying number of the protozoal parasite. It can be well stained by Leishman's stain (Fig. 56).

The specific form of vaginitis caused by *trichomonas* and the enterococcus is extremely difficult to treat. Many methods have been tried, but up to date the most successful method in our hands

has been the insufflation into the air-distended vagina of finely powdered silver picrate-kaolin by a simple bulb and spray apparatus, sold by John Wyeth & Brothers (Fig. 57), or by stovarsol.

The vagina is carefully swabbed as dry as possible, and the insufflator is then used to produce an even deposit of the powder in every crevice and fold of the canal. The patient should lie on the side, inclining on to the abdomen to open the vagina. It is then easily distended by the squeezing the bulb which at the same time sprays the powder.

Insufflation should be done once a week for two or three weeks, and the patient should insert a pessary of silver picrate each night

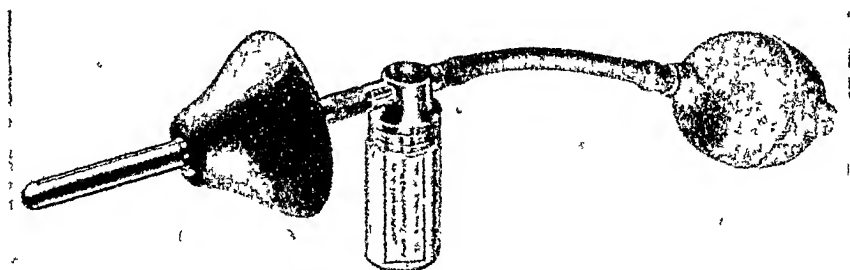


FIG. 57. Apparatus for insufflating the vagina with silver picrate ("picragol") powder. (Messrs. John Wyeth & Brothers.)

for a fortnight. It is claimed that the infection can be entirely abolished within three weeks.

### Mycotic Vaginitis or Thrush Infection

Attention has recently been directed to vaginal and vulval infection by a parasite commonly called *oidium albicans*. The biological examination of this and related organisms has met with great difficulty in classification, chiefly on account of their large number and indefinite biological reactions. A description of the varieties and species of these fungi belongs to the zoologist and is of no practical interest, as yet, to the gynaecologist, though Carter and others (5) after a laborious account of cultural and other characteristics of the different genera and species attempt to correlate clinical symptoms with different genera.

Liston and Cruickshank (6) refer to the uncertainty and confusion in the classification of the large number of "yeasts" and make a plea of selecting *oidium albicans* as the type of organism which infects the vulvo-vaginal mucosa, and "vaginal

thrush" as the name of the disease. Some writers refer to the organism as *monilia albicans*.

Thrush has been found responsible for lesions of the infant's mouth, certain skin lesions and vulvo-vaginitis. Experimental inoculation of the vagina usually produces the characteristic appearances.

The organism can be seen best in a fresh wet preparation and consists of mycelial threads with septate divisions and clusters



FIG. 58 Film of vaginal pus showing the hyphae and blastospores of *oidium albicans*. There are also cellular debris and a large number of organisms.

of blastospores (Fig. 58). They can be stained by Gram's stain or cultured on suitable media.

The conditions suitable for their growth are a moist mucous surface with an acid reaction (pH 4.5), especially if glucose be present. These conditions may be found in the mouths of infants and the adult vagina, especially during pregnancy. From the vagina the organism may spread to the surrounding skin and infect the child later when the patient is delivered.

Vaginal thrush is rare in non-pregnant women, but common

during pregnancy. Thus Carter and others (5) found that "yeast-like fungi" could be obtained from the vagina or vulva of 86 of 200 pregnant women (43%). and Liston and Cruickshank report positive infection in 25% of 200 consecutive pregnant women complaining of leucorrhœa.

The characteristic symptoms are the presence of a discharge which is usually scanty and often curdy, varying degrees of pruritus vulvæ and sometimes soreness of the vulva. Complaint is most frequent during the second half of pregnancy. Examination finds a scanty turbid or almost solid "curdy" discharge, redness of the vulva, and a deep-red congested vaginal wall to which are lightly adherent whitish patches of false membrane. This appearance varies considerably from cases in which there is a small amount of white exudate to those in which the chief physical sign is a membranous deposit. Vaginal examination is generally painful due to soreness of the vulva.

In contrast to the changes caused by *oidium* is the profuse purulent fluid discharge of *trichomonas*. Sometimes both organisms may be found in the same patient.

Diagnosis is established by finding the hyphæ and blastospores mixed with pus and epithelial cells in a film stained by Gram's stain. The floral type in general is usually that known as grade 1, in which the predominating microbe is Döderlein's bacillus. The *pH* of the secretion is between 4 and 5 and seldom above 6. It is therefore of the same order as the *pH* of the normal vagina of the pregnant woman and more acid than the usual *pH* of *trichomonas* infections, which is ordinarily between 5.5 and 6.5. After delivery or during mēnstruation when the vagina is temporarily alkaline or neutral, *oidium* infection and pruritus may disappear. It is characteristic of those uncommon cases of pruritus vulvæ, which report improvement of the irritation only during menstruation, that they suffer from an *oidium* infection.

An important element in vaginal thrush is the presence of carbohydrate either as glycogen in the epithelial cells or glucose in the urine. Iodine staining of the squamous cell deposit always gives a strong brown colour which is also characteristic of a low vaginal *pH*, and vulval thrush is likely to be associated with glycosuria.

The treatment of thrush infections is to swab the vagina dry and clean with saline and then a dry swab, followed by aqueous aniline gentian violet (2%). Under this treatment *oidium* rapidly disappears.



It is convenient under this section to summarise the varieties of leucorrhœa of pregnancy.

1. A discharge, often profuse, consisting of an excess of the normal cervical secretion. It may or may not be the late result of an earlier infection, but it is mucoid in viscosity and white by admixture of an enormous mass of epithelial squames. There are no signs of inflammation, and the discharge does not cause infection after delivery.

2. Pyogenic infection causing a purulent discharge, many pus cells, fewer epithelial cells, few or no Döderlein bacilli, a relatively high pH, and large numbers of various organisms of which an entero-coccus is the chief, and only very rarely a hæmolytic streptococcus. There is a mild vulvo-vaginitis but seldom any sign of infection during the puerperium.

3. Gonorrhœal infection. If this is contracted during pregnancy, there is an intense vaginitis, profuse purulent discharge, and probably some degree of general illness. If it is a chronic infection, there is a purulent discharge and varying success in identification of the gonococcus. There may be little or no local reaction to raise suspicion of the gonococcus.

4. *Trichomonas* is stated by Liston and Cruickshank to be the cause of 40% of all cases of leucorrhœa in pregnancy. It causes a profuse whitish yellow or dirty pink purulent discharge of pH of 5.5, pruritus, soreness and sense of heat and discomfort of the genitalia.

5. Vaginal thrush which we have already described.

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## CHAPTER XI

### SYMPATHECTOMY

THE history of operations for resection of the sympathetic nerve fibres supplying the pelvic organs goes back over forty years, but the more widespread adoption of this branch of neurosurgery in recent times and its special application to the relief of pelvic pain, gives it a claim to inclusion here. It is only comparatively lately that gynæcologists have accepted these operations as an addition to the measures they feel justified in adopting; and though some pelvic surgeons are supporters of the method, others more cautious still remain sceptical and are not convinced that time will prove that the operations yield results of sufficient value to justify the continuance of their performance.

In 1898 Jaboulay (1) tried to relieve pelvic pain by interrupting the afferent pathways in the sacral sympathetic chain in the pararectal region, approach to which was gained by removing the coccyx. In 1899 Ruggi (2) suggested another line of attack on the pelvic sympathetic nervous system, namely by division of the nerves of the ovarian plexus.

Interest in the subject then appears to have languished until 1925 when Leriche (3) made an extensive study of the anatomy and physiology of the pelvic sympathetic nerves and their relation to pelvic pain. He suggested and performed the operation of peri-arterial sympathectomy of the internal iliac artery. Cotte appears to have followed in the same line, but very shortly he (4) advocated the simpler procedure of resection of the superior hypogastric plexus for which he used the description "pre-sacral nerve." This had been the name given to the plexus by Latarget (5), and although the name has been retained it is not good. For we are dealing with a plexus, not a nerve; and its posterior relations are the fourth and fifth lumbar vertebrae and the left common iliac vein, rather than the sacrum. Cotte's first resection of the pre-sacral nerve was in 1924, and since then he has performed the operation over 200 times.

One of the earliest articles on the subject in the English language appears to be that of Fontaine and Herrmann (6), who give a full bibliography, a good description of the anatomy and physiology of the lower part of the sympathetic chain and details

of the operative technique. In this country the most frequent contributor to the literature on the subject has been Davis (7) (8) (9), though by now the operation must have been performed many times by gynaecologists who have not yet published their results.

### Technique of the Operation

For a full description of the anatomical niceties and the technique of Cotte's operation, reference should be made to some article (such as that by Davis (9) ) devoted especially to the subject. It is sufficient here to give a brief outline.

The abdomen is opened by a paramedian incision which may be described as the ordinary gynaecological incision moved upwards for 2 to 3 in. The bowel is then packed off and the two important landmarks, the promontory of the sacrum and the bifurcation of the aorta, identified. A longitudinal incision is made in the posterior parietal peritoneum from just above the aortic bifurcation to the promontory.

The flaps of peritoneum on either side are now lifted up and any attached areolar and nervous tissue is dissected away. The removal of the main bulk of the pre-sacral nerve is then begun. Its complete extirpation entails the excision of all the fibro-nervous tissue between the common iliac arteries and the denudation of both these arteries and of the left common iliac vein. Furthermore there are, as indicated by Meigs (10), one or two fibres from the fourth lumbar sympathetic ganglion which reach the plexus behind the common iliac artery on each side. These must be sought for and divided. It may be noted that all the other fibres reach the plexus by crossing in front of the two arteries.

The operation is not difficult, but it requires painstaking and patient dissection. It should not be hurried. Care must be taken not to include in the tissue removed a length of ureter which has taken up a more mesial position than usual. Difficulty is occasionally encountered from the meso-sigmoid which should lie to the left of the plexus, but which sometimes crosses over it. Injury to the middle sacral artery may also occur and give trouble.

### Functions of the Pre-Sacral Nerve

In broad outline the principal functions of the sympathetic nervous system are the following : it is inhibitor to muscles that extrude visceral contents ; it is motor to sphincters ; it is

vaso-constrictor and glandulomotor. The para-sympathetic nervous system has the opposing actions, viz., vacuo-motor, inhibitor to sphincters and vaso-dilator. When we attempt to apply this generalisation to the pelvis we meet a difficulty. Anatomists tell us on theoretical grounds, that para-sympathetic nerves would not be expected to go to organs derived from the genital ridge. Yet others have stated that para-sympathetic fibres have, in fact, been traced to, and found in, the uterus. If this is confirmed, the origin of these fibres would be from the second, third and fourth sacral segments *viâ* the nervi erigentes and Lee-Frankenhauser's plexus. This point must remain open for the moment. But there is little doubt as to the sympathetic element in the nerve supply of the uterus and other pelvic organs. This comes *viâ* the solar plexus, pre-sacral "nerve" and hypogastric plexuses to the pelvic plexus of Lee-Frankenhauser, above mentioned, in which plexus almost all the nerves supplying the uterus converge.

Interruption of the sympathetic influence on the uterus can most conveniently be achieved by extirpation of the pre-sacral nerve—which henceforth will be called the pre-sacral plexus—or by a direct attack on the plexus of Lee-Frankenhauser. These two lines of treatment will both be discussed. Other methods must also receive brief mention.

It follows from what has been said that the pre-sacral plexus is motor to the uterus (contracting the sphincter and inhibiting the expulsive muscle). It is also glandulomotor and vaso-constrictor. It is probable that it contains afferent sensory fibres and it may be that the relief of uterine pain which is alleged to follow the extirpation<sup>1</sup> of the pre-sacral plexus, results from the division of these sensory fibres. A possible alternative explanation of the relief is that it is in some way connected with the resulting vaso-dilatation or with the alteration in the uterine "polarity." Both of these happenings would be expected either as the result of removal of sympathetic influence or in consequence of the unopposed para-sympathetic action, should this be present.

We are not clear as to the nature of the pain in dysmenorrhœa. Nor is it certain that it is of similar origin to the pain of labour. This matter was the subject of the opening paper by Moir at the Eleventh British Congress of Obstetrics and Gynæcology in 1939. Moir concluded that the pain of labour is not due to muscle contraction but is caused by *stretching* of the lower portion of the uterus and of the cervix. In other words, it is just like the pain

of other hollow viscera. He supported his argument by showing that very powerful uterine contractions in the *puerperal* uterus could be painless. Previously he (11) had suggested that the pain of dysmenorrhœa was of totally different origin and character and that it might be allied to the pain of angina pectoris or of intermittent claudication. He had shown that uterine ischæmia was produced during a contraction in at least some cases of dysmenorrhœa, for he had been able to demonstrate that the force of a contraction of the uterus was, on occasions, greater than the systolic blood-pressure.

It is clear that we have yet a lot to learn about the innervation of the uterus and about the nature of uterine pain. It follows that whatever be the explanation of the relief afforded by pelvic sympathectomy the physiological basis for the performance of that operation is by no means firmly founded. This pelvic neuro-surgery is carried out on what are largely hypothetical grounds. On the claim that it yields good results, rests the explanation of the continued performance by its protagonists.

After the operation the patient's progress, even during the first three days, is remarkably smooth. The bladder and rectum are usually emptied within the first twenty-four hours without any difficulty. There may be a little uterine bleeding shortly after the operation, possibly due to the vaso-dilatation; and, despite the contrary statement in a good many of the articles on this subject, the menstrual loss tends to be rather heavier than previously. Sexual life is stated to be unchanged, and pregnancy and labour appear to proceed in quite the normal and usual manner. In fact some deliveries subsequent to this operation are reported to have been almost precipitate in type; in others less than the usual amount of pain is said to have been experienced.

### Indications for Resection of the Pre-Sacral Plexus

The common indication for this operation is *spasmodic dysmenorrhœa* which has not reacted to other treatments. These need not be detailed here, but it must be emphasised that a major operation such as this is cannot possibly be considered justifiable until every lesser therapeutic measure has been tried. No patient should have this operation performed unless dilatation of the cervix should have been done at least once and possibly twice. It may here be remarked that dilatation of the cervix is said to be a form of sympathectomy. It is suggested that there is a

circle of sympathetic nerves around the external os and that efficient dilatation of the cervix ruptures this.

Other indications that have been taken by various enthusiasts as suitable for the operation of pre-sacral sympathectomy are the following: dyspareunia, amenorrhœa, vaginismus, leucorrhœa, nymphomania, frigidity, pruritus vulvæ and various trophic lesions. If one accepts the statement that the sympathetic is vaso-constrictor and glandulomotor, it will be seen that there is at least some rational thought behind the idea of sympathectomy for some of these conditions. But one must beware of the excesses of enthusiasts.

Others have advocated the performance of sympathectomy in cases of pain accompanying carcinoma of the cervix. The operation has been performed on many occasions for this condition, and has at times yielded fairly satisfactory results. But it will be seen later (p. 242) that a considerably wider sympathectomy than mere resection of the pre-sacral plexus is by some suggested as the minimum procedure from which we may hope to secure relief of the pain of inoperable carcinoma of the cervix. This extended sympathectomy may claim a thorough trial on the grounds that it is a less formidable undertaking than is the operation of cordotomy. In this, the spinal cord is exposed and the antero-lateral columns severed on either side from the ligamentum denticulatum to the anterior nerve root. Moreover, cordotomy is more frequently followed by derangements of micturition.

A more rational approach to the subject of how to deal with the pain of advanced pelvic cancer has been made by the late T. F. Todd (12) who, instead of accepting the recommendation of some who would advocate sympathectomy for these cases, or of others who prefer a direct attack on the sensory tracts in the spinal cord, makes an attempt to distinguish which case is likely to be benefited by one or the other line of treatment. He distinguishes between visceral pain which should respond to presacral sympathectomy; and somatic pain which should be improved by treatment directed to the spinal cord or posterior nerve roots. According to Todd, visceral pelvic pain is of inexact localisation and perhaps diffuse radiation. It is bursting or spasmodic in type and is likely to be intermittent with frequent colicky exacerbations. It is apt to be provoked by functioning of the affected viscus—*e.g.*, after evacuation of the bladder or rectum. It is deep rather than superficial and may be described as "bearing down" in character. In severe cases it may radiate

to the thighs in this way mimicking somatic pain—but radiated visceral pain is nearly always bilateral and localised to the front and upper part of the thighs. Somatic pain in cases of pelvic cancer is a limb pain and is experienced fairly exactly in the distribution of one or more spinal nerves. It is accurately localised and shooting, stabbing or throbbing in type. It may be likened to toothache, is more or less continuous but with periods of exacerbation at night or on movement. There may be an associated hyperæsthesia of the skin in the distribution of the pain.

For the visceral pain Todd is satisfied with pre-sacral neurectomy and does not discuss the extended sympathectomy above mentioned. For somatic pain he advocates intrathecal injection of absolute alcohol as preferable to that formidable operation, cordotomy. This alcohol injection is not "sympathectomy," but a brief description of it in this chapter may be forgiven.

The patient is placed on the side opposite to that on which the pain is felt. The foot of the bed is raised on blocks, pillows are placed so as further to raise the sacral and lumbar spine and the body rotated somewhat ventrally. The posterior sensory nerve roots, which it is aimed to affect, now lie almost horizontally and in the highest parts of the sub-arachnoid space. The point chosen for injection is usually between the tenth dorsal and the first lumbar spine. It must be just above the highest affected nerve root. An ordinary lumbar puncture needle is used and once it is in the sub-arachnoid space 0.5 c.c. to 1 c.c. of absolute alcohol is slowly injected, some two minutes being taken over the process. Not more than 1 c.c. should ever be used and the recommended dose is 0.6 c.c. only. After the injection the patient is kept in the same position for one hour to allow the alcohol to fix. Spinal fluid should not be drawn into the syringe and mixed with the alcohol—this is just what it is wished to avoid. If necessary an injection can be given on the opposite side after a few days interval. Some pain may be felt while the injection is being made but relief soon follows, and Todd states that the average duration of this relief in his cases was five months.

Though Todd's description of the visceral pain in cases of carcinoma of the cervix is a very good one, it should perhaps be mentioned that other descriptions of sympathetic pain are slightly different. Thus Kindel (18) maintains that pain associated with pre-sacral plexus conduction is typically dull and dragging. It

is felt deep in the pelvis and is referred to the rectum, cecum and inner aspects of the thighs. In a case of dysmenorrhœa it may be present, not only at the periods but also between the menses. Pain which is referred to the lumbar regions is not a pre-sacral plexalgia but it may be due to disturbance of the ovarian plexus. Cotte has described a similar reference of sympathetic pain but also includes reference to the bladder as being one of the characteristics of pre-sacral plexus pain.

In an attempt to assess the present views it may be agreed that the type of sympathectomy that can justifiably be performed in certain cases of spasmodic dysmenorrhœa is resection of the pre-sacral plexus. It is also of proved value for certain cases of pain of visceral type in advanced cases of carcinoma of the cervix. Some will even go so far as to think it worthy of performances for intractable leucorrhœa, frigidity, etc. But for trophic lesions of the vulva—particularly kraurosis—it is useless, and for the pain of inoperable carcinoma of the cervix a more extensive procedure is by some, deemed preferable. It is therefore convenient here to consider what are the various operations which can be performed on the sympathetic nerve supply to the pelvic organs.

### Types of Pelvic Sympathectomy

The various types of operative pelvic sympathectomy are:

- (1) Resection of the pre-sacral plexus (superior hypogastric plexus).
- (2) Resection of the ovarian nerves.
- (3) Peri-arterial sympathectomy of the internal iliac arteries.
- (4) Section or partial removal of the lower part of the lumbar sympathetic chain on one or both sides.

Type 1, the operation of resection of the pre-sacral plexus has already received sufficient attention. Type 2 has recently had a fresh lease of life consequent upon O'Donel Browne's article (14). This writer maintains that there is a definite clinical entity, ovarian dysmenorrhœa, which can be recognised by the pain reference and by various tests, including gentle bimanual compression of the ovaries and the passage of an uterine sound. He estimates the occurrence of this type of dysmenorrhœa as 11.0 per cent. of all cases of severe dysmenorrhœa and concludes that these cases should not be benefited by treatment directed to the uterus; and in this he includes pre-sacral sympathectomy. For the true ovarian dysmenorrhœa he advocates bilateral ovarian



denervation. When this condition is associated with uterine dysmenorrhœa this treatment may be combined with Cotte's operation and with the surgical rectification of any abnormal pelvic condition which may be present. His present technique for bilateral ovarian denervation is quite simple and consists of the bilateral division of the infundibulo-pelvic ligaments with their nerves and blood-vessels, at the pelvic brim. The two ends are then securely ligatured and the cut ends approximated by fine peritoneal sutures. Ten completely successful results are claimed to have followed the operation in 16 cases in which it was judged to be indicated. The only two who have married since the operation have had normal healthy infants after normal spontaneous labour. Against this line of treatment is the suggestion by Davis (15) that its wisdom must be called into question since, at least in experimental bitches, it causes profound changes in the follicles, the maturation of which is delayed and incomplete. He does, however, agree that the operation should cure some cases of intermenstrual pain. The subsequent history of the two deliveries in Browne's series of cases should go some way towards dispelling the fear of grave ovarian damage. Possibly the apparent immunity to this is consequent upon sympathetic nerve regeneration, which undoubtedly can occur.

Type (3) operation is no longer done for dysmenorrhœa, but for kaurosis vulvæ and other trophic lesions of the external genitalia, only this operation is of any value. Leriche quotes a case where the cure lasted at least five years and Crainicianu (15) reported several good results in cases of pruritus vulvæ. In the performance of the operation itself, the posterior parietal peritoneum is raised over the internal iliac artery. Some saline solution should then be injected into the adventitia of the artery and the peri-arterial tissues thus distended can easily be removed.

Type (4) operation is an extensive procedure, but good results are claimed for it, and it is stated never to be followed by any motor paralysis or sensory disturbance of the skin, nor by any ascending urinary infection. It is indicated for the relief of visceral pain associated with some cases of inoperable carcinoma of the cervix.

The steps of the operation are :

Incise the posterior parietal peritoneum over the lower portion of the aorta.

Remove all sympathetic fibres of the pre-aortic plexus and pre-sacral nerve from the inferior mesenteric artery to the promontory.

Isolate the right lumbar sympathetic chain just at the lateral border of the inferior vena cava and resect at least two (generally the third and fourth) of the lumbar sympathetic ganglia.

Isolate the left lumbar sympathetic chain which is usually found just beneath the left border of the aorta and resect at least two of the lower lumbar sympathetic ganglia.

### Other Methods of Sympathetic Interruption

Other methods of blocking the sympathetic nerve path have been tried and some are still being persisted with. Binet (17) believed in a 6% aqueous solution of tricoresol of which he injected 30 c.c. into the region of the sympathetic nerve he desired to block. This might be the pre-sacral plexus, the ovarian plexus, its lumbar sympathetic chain, etc. This line of attack, of course, involved abdominal section. More recently Davis (18) has advocated the injection of alcohol into the plexus of Lee-Frankenhauser for dysmenorrhœa. This injection into the plexus itself should theoretically be an improvement on alcohol injection into the parametrium as previously suggested by Bloss (19) and by Young (20). Parametrial injection aims at blocking the uterine peripheral nerves after they leave the plexus and before they reach the uterus.

The plexus of Lee-Frankenhauser is according to Davis, a "bilateral quadrilateral sheet of neuro-fibrous tissue lying on either side of and in front of the ampulla of the rectum." Put in another way, it lies obliquely under the postero-lateral part of the floor of the pouch of Douglas just above and behind the corresponding vaginal fornix. The technique of injecting this plexus involves the administration of an anæsthetic. Then, with the patient in the lithotomy position, one vaginal fornix is exposed, say the right, and the cervix retracted to the left. A long graduated hollow needle is introduced through the vaginal mucosa and passed backwards and outwards for 1.5 cm. at an angle of 45° to both sagittal and coronal planes. A finger in the rectum guides its point to a spot 0.5 cm. from the side of the rectal ampulla. The needle is then withdrawn 0.5 cm. and 1 c.c. of 85% alcohol is slowly injected. The same procedure is repeated on the opposite side. Not many cases are yet reported but a few good results have been obtained. It must be recognised, however, that these injection methods of blocking the sympathetic nerves are still on trial even more than is the operation of resection of the pre-sacral plexus.

## Results

There has not yet been published a sufficient number of results in cases where sympathectomy has been done for the relief of the pain of cancer to justify any detailed discussion here. Indeed, it will at once be seen that the estimate of the degree of success of the operation is entirely in the mind of the surgeon. It will suffice for the moment to say that some surgeons who have adopted this measure are satisfied that it is of benefit and are continuing to perform it.

Again, the operation has not often been done for vulval trophic disturbances, frigidity, etc., and therefore the following figures refer only to the results obtained when the operation has been performed for spasmodic dysmenorrhœa. It must be realised that at the time of the performance of resection of the pre-sacral nerve for this condition any minor gynæcological abnormality that happened to be found was usually corrected. Maybe a small myoma was removed or a retroverted uterus dealt with by shortening the round ligaments. So that even in cases of undoubted beneficial result, this result may have been due to the correction of the gynæcological abnormality and not to sympathectomy.

By far the largest series of cases is that of Cotte, who has now performed the operation over 200 times, and in one series of 125 operations claims to have had 121 "cured" and 3 "relieved." As far back as 1931 (21) he claimed 95% successes in a series of over 100 operations. More recently he has been more modest, and now it would appear that he regards somewhere about 65% as representing his cure rate.

All the other published results are in much smaller series of cases. Thus Fontaine and Herrmann (6) published the results of 22 cases of which 1 died and 6 were lost. Of the 15 cases followed up 13 were well and 2 had received no benefit.

Novak (22) had 7 cases in which the results were completely satisfactory in 6, the remaining patient being improved. Kindel (18) had 89 cases with 2 deaths. Among the 37 recoveries 14 yielded "excellent" results, 4 "very good" and 6 "good." Sellers and Sanders (23) reported 10 cases, of which 6 were relieved, 1 partly relieved, 1 lost sight of and 2 too recent for report. In the discussion following the reading of their paper it was reported that 14 resections of the pre-sacral nerve were performed at the Mayo Clinic in 1935. Their successes were estimated in percentage of cure—thus 9 cases were stated to show 100% recovery, 2 cases

95%, and 3 cases 75%. De Courcy (24) performed the operation 21 times, and all his cases yielded good results. Cannon (25) also had 10 cures out of 10 cases.

More recently Meigs (10) has reported two small series of cases. In one series of 20 cases pre-sacral neurectomy alone was done. Any pelvic displacement, etc., that happened to be found was left. Among these cases there were 15 successful results, 2 partially successful ones and 3 failures. Any case that estimated relief from pain as between 50% and 100% was regarded as successful. The second series consisted of 7 cases that were subjected to pre-sacral neurectomy plus the operative correction of any gynæcological abnormality. Of these, 6 were stated to have had complete relief. The joint procedure is judged to be preferable to neurectomy alone.

In this country, however, operators are usually not quite so optimistic about their results. Davis, in a personal communication, states that his cases show a 60% "cure" or "considerable relief" rate. This is an improvement on the 50% which he claimed in 1934, and is certainly better than the mere 24% at which he rates his successes with dilatation of the cervix. Donaldson also in a personal communication gives his results in 54 cases followed up. Among these he has 18 (or 33%) "good" results; 16 (or 29.6%) "fair" results and 20 (or 37.1%) "bad" results. But he sets a strict standard whereby the grading of the results is assessed, and he bases his classification on the ability to work during a period time. For example, a patient who states "I am glad to have had the operation but feel I should be a lot better" is classified as "bad." Another who says "the pain is not quite so bad" is also classified as a bad result because she is unable to work during a period. Donaldson concludes that the operation is more successful than dilatation and curettage, but that the lesser operation should be tried first, especially if the uterus is of normal size. It is worthy of note that the operation appears to be one that can be performed with reasonable safety, though it is seen above that Fontaine had one death and Kindel two. These two were both from post-operative pneumonia. Generally speaking, however, the progress of these cases after the operation is remarkably smooth, and if, after the passage of time, it is still found that the results are anything like as good as those at present claimed, and if it is found that the benefits conferred are permanent, then it would appear that in pre-sacral sympathectomy we have a surgical measure which is likely to be

of great value in the treatment of those cases of dysmenorrhœa which, resistant to lesser therapeutic measures, continue to make almost intolerable the life of the victim. But the "ifs" in the above statement are significant. In our experience the operation is not so universally successful as some would have us believe.

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## CHAPTER XII

### THE SEX HORMONES

IN the last edition of this book we referred to the increasing complexity of knowledge of the hormonal system. If it was true in 1939, it is doubly true to-day, despite the generally inhibiting effect of the war on much physiological research. The mass of material that is published in the journals is almost impossible to digest except by one whose whole time and thought is spent in the study of comparative endocrine physiology. A glance at the contents page of journals devoted to endocrinology gives an idea of the magnitude of this research, its widespread zoological range, the artificial or unnatural conditions of many of the experiments and lastly, the absence of articles of the "integrating" type. We find such titles as "Occurrence of Estrogens in the Ovaries of the Winter Flounder," "Blood Serum and Skeletal Changes in Two Breeds of Ducks Receiving Estrogens." "The Effect of Experimentally Induced Pseudopregnancy upon the Survival of Adrenalectomised Cats." Taking the contents bill of one endocrine journal at random we find that of twenty-eight articles only four were devoted to the problems of human physiology. The remainder described studies on animal physiology which may or may not have any bearing on human problems. It is well that all possible scraps of knowledge should be collected. The most unlikely material has often proved to be the basis for striking advances in medicine, but it is permissible to ask how far the isolated results of many present-day researches in endocrinology can be of value unless they are simplified, classified, and, as we have said, integrated.

There is also a tendency, especially on the part of laboratory workers to apply the results of their experiments on animals, usually far distant from the human species, and often "abnormalised" by some severe pre-experimental operation, to the clinical problems of men and women. The fact that there is disappointment in the value of sex hormone therapy for common clinical disorders is evidence of the fallacy of this assumption that animal experimental results represent similar processes in man. There are many profound differences in the action of the hormones in different animals.

In addition to research in the wide field of comparative

ocrine physiology, we need more work on the special human problems by clinical observation. If, therefore, we may be permitted to make any criticism of the fine work of a body of men and careful investigators, it is that perhaps too much attention has been devoted to the laboratory animal and not enough to the reactions of the human organism.

At the beginning of a new branch of physiology—largely covered and elaborated by the early experiments on animals—is inevitable that physiological analogies should be drawn, but it is gradually learnt that there are differences in the reactions between even the rat and mouse (*e.g.*, oestradiol benzoate), and how much more between man and the small rodents.

Recently, especially since cheaper synthetic compounds have come available in sufficient and accurate dosage, it is true that more clinical research has been carried out. The results have been somewhat disappointingly disappointing, but nevertheless, some real and defined additions to our therapeutics have been gained. Certain general principles have emerged from the mass of investigation. One of the most important is the idea of the primary gland (the anterior pituitary body) producing its primary hormones—apparently of great chemical complexity—which stimulate the secondary glands (vary, thyroid, testis, adrenal, etc.) to produce the secondary hormones. These hormones are comparatively simple chemical bodies and act directly on the viscera, glands, nutrition and metabolism.

An interesting speculation for those who are clinicians, rather than chemists and biologists, is the point in the endocrine chain at which the influences derived from emotional states and the nervous system impinge. While surrounded by the results and deductions of the pure chemists and animal biologists, it is necessary for us to remember that in clinical medicine the subject is not a lowly organised laboratory animal, but one whose physiological processes are conspicuously under the daily influence of his or her feelings. The endocrine system is not an exception in susceptibility to these influences, and while its implements are the substances prescribed by the chemists, yet the control of the machine may be varied by the operation of psychological factors.

### THE CHEMISTRY OF THE SEX HORMONES

The hormones secreted by the gonads belong to the chemical group of sterols. The parent substance from which they can be derived is the inert sterol cholesterol, and their structure is the

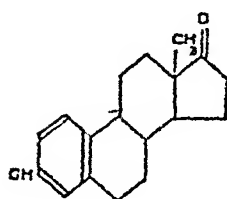
arrangement of benzene rings in the cyclopentenophenanthrene system. By insertion of methyl, hydroxyl, alcohol or ketone radicles, an immense number and variety of hormonally active substances can be made. For example, E. C. Dodds states that sixty androgenic compounds have already been prepared by the organic chemists. The chemistry of the sterols and their hormonal derivatives is extremely complex and is unsuitable for further description in this book.

Nomenclature of the œstrogenic hormones is a difficulty in any clinical description of their actions and uses. Throughout this chapter the word *œstrogen* is used to include all the œstrus-producing substances, especially in relation to a qualitative effect. The words *œstrone*, *œstriol* and *œstradiol* are used for the specific substances to which these names have been allotted.

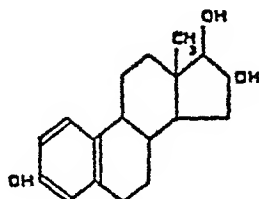
### THE ŒSTROGENIC HORMONES

Though this group is intermediate in the chain, we will consider it first, as its discovery gave great impetus to the study of the whole series.

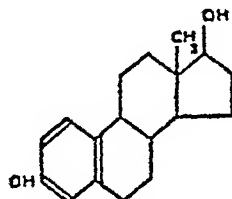
It was first noticed by Frankel that if the liquor folliculi of the Graafian follicle was injected into mice it produced evidence



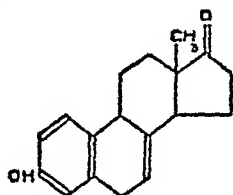
ŒSTRONE



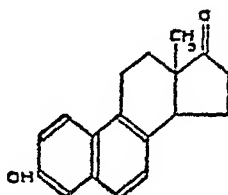
ŒSTRIOL



ŒSTRADIOL



EQUILINE



EQUILENINE

of œstrus, but it was not until 1917, when Stockard and Papanicolaou discovered the technique of the vaginal smear examination as a test for the presence of œstrus, that the effects of the œstrogenic hormone could be examined and measured with



accuracy. Since the publication of their work our knowledge of these hormones has made great progress.

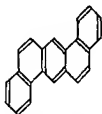
In 1927 Aschheim and Zondek found an œstrogenic hormone in the urine of pregnant animals, and later it was discovered in large amounts in the placenta. To-day we know five œstrogenic hormones which have been isolated from the ovary, urine and placenta. At first it was thought that the œstrus-producing hormone was produced only by the Graafian follicle, but Parkes showed that œstrus still occurred in mice after they had been subjected to a dose of X-rays sufficient to destroy the follicles, but that when the ovaries were removed œstrus ceased at once. This observation provided evidence that the substance is produced by the non-follicular cells of the ovary and possibly, as some think, by the corpus luteum.

In order to show the chemical relationships of the œstrogenic hormones, we give, on p. 240, the formulæ (taken from Dodds, *B.M.J.*, February 20th, 398, 1938).

œstradiol is the substance secreted by the ovary, while the degradation products œstrone and œstriol are found in the urine and placenta respectively.

œstradiol is five times as potent as œstrone and œstriol when administered to the rat, but is of equal potency when given to the mouse. Such variations of action in small animals illustrate the uncertainty of direct application to man of results obtained from animal experiments, without clinical corroboration.

The œstrogens are related to the carcinogenic substances found in coal tar, two of which are given below :—



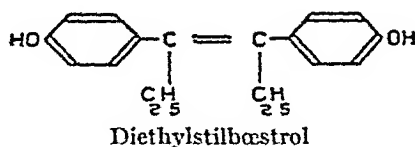
1:2 benzanthracene. 1:2:5:6 dibenzanthracene

and also to the bile acids, cholesterol and ergosterol. The relationship between the œstrus-producing and cancer-producing agents is apparent from a glance at the chemical structure, and it was soon discovered that the œstrogens can produce cancer of the mamma in a sensitive strain of inbred mice, and that many

of the carcinogenic hydrocarbons are capable of producing œstrus. A further interrelationship is that methylcholanthrene, easily derived from a bile acid, is a powerful carcinogenic substance.

There is, however, an important difference in the carcinogenic powers of the œstrogens and the true benz-anthracene group of carcinogenic substances. Whereas the latter will produce epithelioma when painted directly on to the skin, œstrogens will not do this, but will *prêdispose* to the growth of carcinoma in the mamma of mice if large quantities are injected from birth. There is some evidence accumulating that large and prolonged administration of the œstrogens may produce human cancer.

A result of the synthetic chemistry of the œstrogens is the production by Dodds and Lawson (1938) of a comparatively simple substance—diethylstilbœstrol.



It has œstrus-producing effects on laboratory animals about two and a half times greater than that of œstrone.

A convenient substance having a still higher œstrogenic potency is dihydro-stœthbœstrol (hexœstrol). These substances show that the œstrus-producing character is not limited to the phenanthrene ring system.

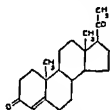
The amount of the œstrogen in the Graafian follicle has been estimated by Zondek at about 2 mouse units per cubic centimetre of liquor, but it is probable that the retention cysts of unruptured follicles contain a higher concentration. Œstrogens have not been found in the fluid of ovarian tumours (cysts), with the exception of the granulosa-cell tumour and xanthofibroma, which contain large amounts and cause irregular uterine hæmorrhage.

The œstrus-producing hormones are soluble in fatty vehicles, and to a less extent in an alcohol-alkali medium.

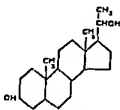
## PROGESTERONE

In 1929 Corner and Allen found that injection of an extract of corpus luteum into œstral rabbits produced pseudo-pregnancy changes of the endometrium, but only if the endometrium had previously been influenced by an œstrogenic hormone. In 1934

Butenandt succeeded in obtaining the active substance in crystalline form, and now it can be produced synthetically from the inert sterol of the soya bean.



PROGESTERONE



PREGNANDIOL

The hormone as secreted by the corpus luteum is called *progesterone*, and it is excreted in the urine as *pregnandiol*, which is biologically inert. The activity of all excretion products of circulating hormones is always much less than that of the parent substance.

Progesterone is fat soluble and is not absorbed when taken by mouth. Recently Inhoffen has prepared a derivative, *pregneninolon*, by introducing the ethinyl group ( $-\text{C} \equiv \text{CH}$ ) in place of the  $-\text{CO} \equiv \text{CH}$  radicle of the progesterone molecule. This substance is absorbed and active when taken by mouth. By the preliminary use of stilboestrol followed by *pregneninolon*, the menstrual cycle of the endometrium can now be produced by oral administration (Dodds).

### THE GONADOTROPIC HORMONES

Research on the hormone activity of the pituitary gland is showing it to be of almost unbelievable complexity. The comparatively simple oxytocic and pressor substances of the posterior lobe have long been known, but during the last twenty years the functions of the anterior lobe have been explored with the result that over a dozen different hormone activities have been described. The very large amount of investigation devoted to the anterior pituitary lobe has led to a mass of isolated and as yet unco-ordinated descriptions of functions which are often confused and sometimes contradictory. It is uncertain whether different groups of workers are describing the varied activities of the same hormone or a number of hormones. The situation is becoming further complicated by the suggestion of anti-hormones and the possible relationship of the vitamins to the hormonal system. In

addition to the gonadotropic hormones, it seems that the anterior lobe exerts at least fourteen other hormonal effects by substances which may be specific for each effect or multiple in their action. Some of these effects are (1) control and stimulation of general growth of the whole body, probably acting primarily through the skeleton; (2) thyrotropic action, whereby the thyroid is altered histologically with a corresponding increase of liberation of its secretion. The thyrotropic substance by its influence on the thyroid, can, when injected, produce the various symptoms of thyrotoxæmia, but also it has been shown that some of the effects (increased basal metabolic rate and exophthalmos) can be produced by the extract of the anterior pituitary after thyroidectomy; (3) Stimulation of mammary secretion by a substance called *prolactin*, which can be obtained as a pure crystalline body. It acts only on the fully mature mammary gland. (4) Inhibition of adrenalin hyperglycæmia and insulin hypoglycæmia. (5) Trophic action on the adrenal cortex; (6) Retention and increase of carbohydrate store; (7) An adrenal corticotropic effect, and other effects of less direct interest to the gynæcologist as far as we know at present.

In this chapter we will confine ourselves to a few remarks on the gonadotropic hormones.

It was demonstrated that removal of the hypophysis was quickly followed by genital atrophy in both sexes. In 1921 Evans and Long showed that extracts of the anterior lobe of the pituitary body caused luteinization of the ovary, while if the same gland were implanted under the skin of the animal's back, the opposite effect was produced, namely, the suppression of the corpora lutea and enormous production of Graafian follicles. If implantations are made into immature animals, they are immediately brought into a state of precocious œstrus, though if coitus occurs at this time pregnancy never follows because there is no actual ovulation. Such animals show no induced changes in their pituitary glands, and, if the implantations are discontinued, the animal reverts again to its immature state. It is curious that extracts of the anterior lobes of *immature* animals and also of male animals have a power equal to or even greater than that of the pituitaries of mature females in provoking the ovarian changes described above.

The relative amounts of the two hormones which can be extracted from the anterior lobe vary in different animals. The luteinising hormone is the chief factor in the pituitary gland of

the pig and sheep, while from the horse can be obtained a large amount of the follicle-stimulating hormone. It was thought at first that there were two gonadotropic hormones, one of which stimulated maturation of the ovarian follicles (prolan A), while the other, secreted in women during the second half of their cycle, stimulated the luteinisation of the ruptured follicle (prolan B). Evans now considers that there are four sex hormones to be obtained from the anterior lobe, as follows :—

- (a) The follicle stimulation hormone.
  - (b) A follicle-luteinising factor, capable of converting the non-ruptured follicle or the corpus hæmorrhagicum in a corpus luteum.
  - (c) An interstitial cell-stimulating substance, capable of stimulating the ovarian interstitial cells to secrete an œstrogenic hormone.
  - (d) An inhibiting substance.
- (Quoted from E. C. Dodds, *Lancet*, ii., 15, 1939.)

It is claimed by Astwood that the anterior pituitary secretes three gonadotropic hormones. In addition to the follicle-stimulating and luteinising hormones, he adduces evidence to show that a luteotropic ("luteotrophin") hormone is necessary to maintain the secretion of progesterone by the corpus luteum.

In addition to the female hormones the anterior lobe also secretes several gonadotropic hormones which influence the maintenance of function of the male genital apparatus.

The chemical constitution of these substances is not known except that they are protein molecules with a carbohydrate moiety.

Attempts to isolate the gonadotropic hormone from the anterior pituitary have met with little success, but similarly acting substances have been prepared from the urine of pregnant women at about the third and fourth months, and also from the serum of the pregnant mare in the first half of pregnancy. The first, manufactured and sold under the names *Antuitrin-S*, *Pregnyl*, *Gonan*, etc., is an "anterior-pituitary-like" substance, dissolved in a protein solution, having chiefly a luteinising action; while the second—sold under the names of "*Serogan*," *Antoslab*, etc.—is credited with a follicle-stimulating function.

The luteinising hormone of the urine of pregnancy (and of other fluids and tissues of the body during pregnancy) is also found in the urine of women after the menopause, but that

which is obtained during pregnancy differs in some way from that obtained from the urine of post-menopausal women, or those who have had both ovaries removed.

The origin of the anterior-pituitary-like hormone of pregnancy urine is probably the chorionic elements of the placenta. Evidence of this is the excretion of excessive amounts of this luteinising hormone by patients suffering from chorion-carcinoma or hydatidiform mole. It is the presence of this substance—the luteinising hormone—in the urine of pregnancy which is responsible for the well-known tests for pregnancy. During pregnancy the gonadotropic functions of the anterior pituitary are subdued by the large amount of circulating oestrone, and it is possible that the chorionic tissue replaces the function of the anterior pituitary.

### THE MALE HORMONES

Knowledge of the testicular hormones began with the observation of Berthold in 1849, that injection of testicular extract into the capon would stimulate growth of its comb. Progress was held up for a time by the fact that the testis contains only a very small amount of androgen, but Butenandt was successful in isolating a hormone—androsterone—from human male urine. The urinary androgen was found to be feeble in its action compared with the substance isolated from the bull's testis—testosterone—which is about ten times as potent as androsterone. The potency of testosterone is considerably increased by conversion to the propionate ester, which is the preparation used in clinical work. Both hormones can now be produced synthetically from cholesterol. Androgens are excreted in large amount in men's urine and in the urine of pregnant women, but in quite small quantities in the urines of male animals. The actual amount of excretion is variable within wide limits from day to day, and no conclusion should be drawn from estimates of urinary androgen for less than four or five days. The amount of androgen in the urine is enormously increased in patients suffering from adrenal tumour, and is a useful aid to diagnosis in doubtful cases. The physiological effect of the androgens is to initiate and maintain the growth of the secondary sex characters of the male. They are capable of restoring in part the atrophy of the sex organs which follows castration and they stimulate descent of the testicles and of penile growth.

It is important, however, to remember that both the androgens

and gynæcogens are bi-sexual in their effect. Thus either group of hormones may produce varying effects on the reproductive system and functions of the opposite sex. Examples of the dual origin and functions are the presence of large quantities of œstrogen in the urine of the stallion and androgens in human female urine.

Hill and Strong have shown that the implantation of normal ovary into castrated males will maintain the secondary sex characters of the castrated male. Abarbanel (*American Journ. Obstet. and Gynæc.*, 39, 246, 1940), gives in tabular form a comparison of the effects of testosterone, œstrone and progesterone on various sexual structures and function. It is clear that testosterone exerts considerable sexual effects on the female genital system and temporarily assumes the functions both of œstrone and progesterone in varying degree in different instances.

#### Functions of the Œstrogenic Hormones

The outstanding effect of these bodies is to produce œstrus in the immature, senile or spayed female. In rodents this condition can be watched with exactitude by examination of the "vaginal smear." In women also the vagina shows changes—though not so marked—which indicate the presence of œstrus. The "smear technique," consists of making a film on a microscope slide of a scraping of the vaginal wall by a platinum loop. During œstrus the vaginal wall becomes cornified by great proliferation of the squamous layers of the vaginal epithelium, so that the smear taken at this time is largely made up of enormous masses of flat squames with no obvious nuclei. During the ancestral period the squamosa is normally thin and cornified, and the smear will show a relatively small number of squames and a correspondingly large number of leucocytes. In the human vagina during œstrus the superficial cells contain large amounts of glycogen—as shown by the dark brown staining by tincture of iodine during the cleansing process before vaginal operations—and a thick, rugose and pale pink vaginal wall. There are also other details, such as the profuse, clear cervical mucus of thin viscosity and a relatively open internal os uteri.

If œstrogen is given to immature animals the sexual organs will grow to full maturity before that of the somatic growth, and in senile animals a similar change is observed.

After the denudation at the time of menstruation, œstrogen stimulates endometrial growth and proliferation of the cells,

notably those of the glands. The gland nuclei lie at the bases of the cells; there is no glycogen in the cells and no mucin in the lumina of the glands. The stroma cells which are loosely packed at the end of menstruation become arranged more densely as the follicular (œstral) phase develops.

Not only does œstrogen affect the growth of the uterus and other genital organs, but it influences uterine function by increasing its sensitivity to the posterior pituitary extract, whereby it is rendered more contractile and amenable to the effect of direct oxytocic stimulation. It is probable that this action involves also the Fallopian tubes and that they become increasingly sensitive as ovulation approaches. It is possible that a hyperactivity of the tubes at this time, amounting to actual "colicky" spasm, is the cause of much of the "middle pain" which sometimes troubles women at the middle of their monthly cycle.

Œstrogen also has important effects on other glands. Above a certain threshold value, it is believed to inhibit the formation of the corpus luteum, and it exercises an inhibiting effect on the gonadotropic activities of the anterior pituitary lobe.

The new substances—**diethylstilbœstrol** and **hexœstrol**—discovered by Dodds and his fellow-workers have an œstral activity two and a half times that of œstrone. The action on ovariectomised rats, on the mating, on the vagina and uterus of immature rats, on the uterus of immature rabbits, and on the feathers of capons, is similar to that of œstrone. Nipple growth in the guinea-pig is of the same order as that caused by œstrone, but it appears to have less stimulating effects on the mammary tissue.

There are, however, differences between the synthetic preparation, stilbœstrol, and the natural products œstradiol and œstrone, both specific and non-specific. For example, Von Haam and others have shown that the growth of the uterus of experimental animals (immature mice) increases almost identically up to doses of 20 $\gamma$ , after which the weight of the uterus declines sharply with stilbœstrol therapy, losing nearly half its gain, compared with a maintenance of weight under the influence of œstrone up to doses of 200 $\gamma$ . The effect on the uterus and certain glands of adult animals also varied. Stilbœstrol caused a greater increase in weight of the uterus, pituitary and adrenal than did œstrone, but the weight of ovary and prostate showed little difference. The cellular changes of the pituitary gland also differ under treatment by the two drugs.



High doses of stilboestrol administered to animals are toxic and even fatal, some animals being more susceptible than others. Compared with the amount of the various doses lethal to animals the average human dose, up to 5 mgm. a day is well within the bounds of safety. Pathological changes under continued dose of 0.1 mgm. three times a week in rats are chiefly a fall in hæmoglobin, and red cell count, and parenchymatous degeneration in liver and kidneys.

The œstrogens—as has been stated above—are excitants of uterine activity. This is manifest in the sensitising effect which they have upon uterine muscle in the presence of posterior pituitary extract (pitocin). A subminimal dose of pitocin can be made to produce a strong contraction of the uterine muscle of the guinea-pig, provided œstrogen is previously added to the fluid medium in which the muscle is suspended. Large doses of œstrogen will produce abortion or resorption of the foetus of rodents if given in early pregnancy, but no amount of it will cause abortion in women. Further, when given towards the end of pregnancy, or even on the verge of labour, it does not seem capable of inducing labour. In women it is not easy to demonstrate that œstrogen will render the uterus more sensitive to the action of pitocin immediately before labour, but there is some evidence that administration of œstrogen followed by pitocin has an influence on the stimulation of uterine contractions during early labour.

In addition to the more specific effects of these hormones which can be demonstrated by exact experiment, there is clinical evidence that they have a generally stimulating effect on metabolic activity. Some cases of post-menopausal granulosa cell tumours describe a sense of well-being which is manifest by the increased activity and buoyancy of the patient, changes which are certain to disappear after the removal of the tumour.

### Functions of Progesterone

The essential activity of this substance is to convert the endometrium from its phase of œstral proliferation into the secretory phase in preparation for the embedding of the fertilised ovum. The endometrium becomes thicker and more vascular. The glands secrete mucin, become more tortuous, and contain tufts of cells, having a clear basal zone in which is deposited glycogen. The stroma cells are polygonal and crowded together, suggesting the appearance of decidua.

So long as the corpus luteum remains in control, the mucosa of

the uterus remains intact, but, in women, it breaks down into a menstrual discharge about thirty-six hours after the gland is removed from the ovary. These changes in the endometrium, characteristic of the effect of luteal activity, can only be induced if the endometrium has been under the previous influence of the œstrus-producing hormones. It appears that true menstruation, therefore, is the result of bi-phasic endometrial changes which have been induced, in turn, by the influence of œstrogen stimulation, followed by that of the corpus luteum. Clinical evidence of this fact was demonstrated by the work of Kaufmann, who showed that true menstruation could only be induced in senile women if the period of *œstrogen* injections was followed by a period of injections of *progesterone*. It is true that uterine bleeding will follow a week or so after giving large doses of œstrogen without the succeeding administration of progesterone—the so-called “œstrone-withdrawal” hæmorrhage—but microscopy of the blood discharge does not reveal the particles of endometrium in the secretory phase—the shedding of which is the only evidence of true menstruation.

Progesterone exerts an inhibitory action on uterine contractility in contradistinction to the action of œstrogen. After the fertilisation of the ovum the corpus luteum grows and presumably increases its inhibitory action. It also stimulates the growth of the uterus. But after the middle of pregnancy the gland seems to atrophy, and during the latter months it is composed of degenerate vacuolate cells. It was once believed that the onset of labour was probably due to the withdrawal of the inhibitory action of progesterone consequent upon degeneration of the corpus luteum at the end of pregnancy, thus leaving the way open for the excitant and sensitising effect of œstrone. But in view of later facts, this simple explanation is insufficient, and we must yet search for the cause of the onset of labour.

But not all apparent menstruation is true menstruation, inasmuch as it follows the degeneration of a corpus luteum arising from an ovulating follicle. “Menstruation” can occur regularly without preceding ovulation—so-called anovular menstruation—and therefore in the absence of a corpus luteum. This form of bleeding is probably an “œstrone-withdrawal” hæmorrhage. It can be prevented by giving progesterone, but, again, bleeding will occur—probably true menstruation—about four days after the cessation of the injections of progesterone.

The understanding of the menstrual cycle is further complicated

by the fact that, though progesterone is produced from the moment of ovulation, the formation of œstradiol is continued in increased amount up to the beginning of menstruation, when it falls abruptly.

Menstruation, therefore, may be the result of failure of production of progesterone by reason of necrosis of the corpus luteum, or when the level of the blood œstradiol falls below a certain threshold value.

It is postponed by administration of œstrogen, but only when it is given before the date of ovulation. This appears to be explained by its action on the anterior pituitary body, whereby the ovulation-stimulating gonadotropic hormone of the latter is inhibited. But large doses of progesterone, when given to normal women during the pre-menstrual period do not delay the onset of menstruation, and even when the corpus luteum is removed (during laparotomy) from normal women at this time, the administration of progesterone, even in large doses, does not hold off the premature menstruation, precipitated by the operation. It may delay it for a brief or variable time, but it is not possible to delay the onset until the time of the next normal menstruation.

In animal experiments it is possible by the administration of progesterone to maintain the passive condition of the uterus at the end of pregnancy and so delay the onset of labour. There is evidence that premature expulsion of the human ovum can similarly be prevented in certain cases, but labour cannot be delayed in women at term.

It has been noted that complete absence of pregnandiol in the urine during early pregnancy indicates an impending abortion, but at the same time abortion may occur if its excretion is normal. Normally the amount of pregnandiol in the urine is increased during pregnancy. This fact may be used as a means of diagnosis of pregnancy if the test is applied during a period of amenorrhœa.

The amount of pregnandiol in the urine is also depressed in cases of toxæmia and nephritis.

### Functions of the Gonadotropic Hormones

As far as we can see at present, the functions of these hormones in woman are as follows :—

The follicle-stimulating hormone (prolan A) begins to operate at or about the time of menstruation. Under its influence a Graafian follicle is matured, but the formation of the ovum within the follicle is not within the function of prolan A. With

the maturation of the follicle is formed oestrogen in increasing amount until the period of rupture of the follicle. It may be that the process of rupture is also controlled by yet a further pituitary hormone. After rupture of the follicle, the pituitary ceases to secrete prolan A and turns over to the production of the luteinising hormone (prolan B). The effect of this substance is to stimulate the growth of the corpus luteum, but it may be that the secretion of progesterone is maintained by a "leuteotropic" hormone named by Astwood "luteotropin." If the ovum is not fertilised the corpus luteum degenerates, again by influence of declining secretion of prolan B, on or about the twenty-sixth day of the cycle.

That there must be more than the two prolan hormones controlling ovarian function is shown by experiments on rats and sheep. The persistent corpora lutea of hypophysectomised rats do not secrete progesterone, as shown by the absence of endometriotropic changes, and cannot be made to secrete by the injection of either the follicle-stimulating or luteinising hormones. But if the rats are injected with the pituitary fraction—luteotropin—secretion of progesterone follows. Astwood states that luteotropin is closely related to the lactogenic and adrenotropic hormones.

The ovary also reacts on the pituitary activities. After ovulation and with the formation of the corpus luteum the further secretion of the luteinising hormone is inhibited by the action of progesterone; and oestrogen, produced in the follicles during the ripening stage, gradually inhibits the secretion of further follicle-stimulating hormones, and stimulates the production of luteotropin.

Such, in brief, is the story of the pituitary and ovarian cycles. It is certain that the details vary in different animals, and it would be wrong to assume that the mechanism of the human menstrual cycle has been finally described, inasmuch as many of the observations on animals have been directly applied to human physiology. But gradually the riddle of the oestral or menstrual cycle is being solved despite the exaggerated importance attributed to the results of experiments on animals as contributions to knowledge of human physiology.

#### Standardisation and Dosage

**Oestrogens.** Much confusion has been caused by different standards of unitage, but now it is agreed that 1 international unit of oestrone should be the equivalent of  $\frac{1}{10,000}$  mgm. of crystalline

œstrone. The benzoate unit is 10.000 mgm. of crystalline œstradiol benzoate.

These hormones can be given by injection, by the mouth, through the skin or through the vulval and vaginal mucous membrane. The absorption capacities of these different routes vary. For example, Zondek states that absorption through the skin in the form of an ointment requires seven times as much œstrone to produce œstrus in mice as when given percutaneously, but if it is given dissolved in benzol, ether or 96% alcohol, it is rapidly absorbed, and is as effective as the same amount given under the skin. Delay of absorption, allowing a "spread-over" of the effect of the hormone, is obtained by injecting an oily solution, or by subcutaneous implantation of crystalline œstrone.

œstrone assay of the urine gives variable results and cannot be depended upon to give a reliable idea of the use or rejection of œstradiol in the body. Thus, when œstradiol was given to ovariectomised women, the urine assay showed only 8% to 12% of it excreted in the urine during the next two days. In any case, to form an idea of urinary œstrone excretion, in the presence of abnormality, it would be necessary to estimate the excretion every day for a month, which is manifestly impossible in clinical work.

**Progesterone.** This hormone is standardised by the amount required to produce a certain degree of endometrial proliferation in the rabbit after a previous treatment by œstrogen. This amount is stated to be 1 rabbit unit (1 mgm. is equivalent to about one rabbit unit), and is  $\frac{1}{2}$  an international unit. A clinical difficulty in obtaining results by administration of progesterone is the relatively small dose when applied to women. Further chemical researches may make it possible to cheapen the product and enable larger doses to be given. The dosage is usually described in milligrammes instead of units.

**Gonadotropic Hormones.** As we have stated, the fraction which is mainly luteinising in action is obtained from the urine of pregnant animals, while the follicle-stimulating factor is obtained from the serum of pregnant mares. Though these are not the actual substances identical with the hormones secreted by the anterior pituitary body, yet there is evidence that they have a greater physiological activity. For example, the anterior-pituitary-like substance in the urine produces a greater growth and distension of the rabbit's uterus than the hormone obtained from the gland.

The urinary hormone is standardised by the production of hæmorrhagic points in the ovaries of the rats, and is sold in doses of from 30 to 500 units. The serum gonadotropic hormone is sold in doses of 100 units.

### Therapeutic Applications

Our knowledge of the chemistry and physiology of the sex hormones has far outstripped our capacity to apply it in clinical medicine. There have been many disappointments in the results of clinical treatment because the physiological processes observed in animals are not necessarily those which obtain in women. Not only are there many fundamental physiological differences, but the doses of the hormones available have been described and administered in terms of small animals, though this difficulty has been recently overcome in the case of some of the hormones. But perhaps the chief cause of disappointment has been the indiscriminate administration of hormones in totally unsuitable cases. This has arisen partly from the difficulty and complexity of the whole subject of endocrinology, and partly because of the extravagant claims of therapeutic success made by some of the manufacturing firms. And here perhaps we might be allowed to urge that the manufacturing firms would contribute much to the future success of sex hormone therapy if they could agree among themselves to adopt uniform chemical names for identical chemical products, which are at present sold under many different trade names. The confusion of nomenclature, caused by the drug manufacturers, greatly increases the difficulty of hormone therapy.

In this section we propose to indicate only those conditions for which the success of hormone treatment has become established by real clinical observation. There are many other conditions for which success is claimed in some quarters, but for which the treatment has been uncontrolled and imperfectly observed.

Hitherto, because of the advance of chemical knowledge, œstrone or its derivatives has been chiefly employed in clinical work, but as the gonadotropic hormones become more easily available, and in more adequate dosage, it is probable that they will largely displace the use of œstrone, which is often used at present for wrong indications.

Collip draws attention to an important new principle in endocrine physiology which may have influence in therapeutics. He states that there is evidence of the production of *anti-*

*hormones.* It has been known that prolonged treatment of animals with some hormones excites a resistance to the action of the hormone. This has been shown to be true of the gonadotropic, thyrotropic and growth hormones. The mechanism may be that of an immunity factor or liberation of an already existent specific anti-hormone. The therapeutic importance of these facts is that the principle may be applicable to other than pituitary hormones, such as œstrogens, and that after a point further treatment may be useless in so far as the production of the anti-hormone has been stimulated.

It was hoped that estimation of hormone excretion in the urine would serve as a guide to the particular hormone which is deficient in the circulating blood, but now we know that the amount excreted bears little relation to the amount in the body. Further, they are excreted in different chemical form from that in which they are secreted by the glands. For example, the ovary secretes œstradiol but the substances appearing in the urine and placenta are œstrone and œstriol, which are only about one-fifth as potent as the parent substance. If œstrogens are injected into oöphorectomised women, less than 15% can be recovered from the urine. Progesterone is converted into pregnandiol and is excreted in the urine as such but less than half of the amount of progesterone administered can be recovered as pregnandiol. Callow states that the androgenic hormones are destroyed to such a degree as to render urinary estimations valueless. Similarly, the pituitary substances are excreted in so small amount after injection that no useful deductions can be made from urinary assay.

### Indications for the Use of the Œstrogens

There are four main groups of clinical conditions for which these hormones are of proved value.

*Inflammatory states of the vagina after the menopause or before puberty (vulvo-vaginitis of children).* So-called senile vaginitis is caused by a pyogenic organism. The protective influence of lactic acid produced by Doderlein's bacillus has been lost. This is, in its turn, probably due to the almost complete absence of glycogen in the superficial squames of the vaginal epithelium. A further predisposition to pyogenic infection is the thinness of the vaginal epithelium. One of the effects of circulating œstrogen before the menopause is to maintain a high cellular content of glycogen, and when, after the menopause, this influence is with-

drawn, the vagina loses its resistance. The administration of œstrone or stilbœstrol to these patients without any local treatment usually cures within two or three weeks. An exception is the trichomonas infection which can cause vaginitis at any time of life, irrespective of the presence of Döderlein's bacillus. Œstrone has no effect on clearing this form of vaginitis, either before or after the menopause. Senile vaginitis is a distressing condition, for which all ordinary treatment such as douches and applications of silver nitrate are disappointing, but it quickly yields to œstrone or stilbœstrol.

A technique suggested is to give 100,000 units of œstrone in small doses during one week, or 3 mgm. of stilbœstrol each day for ten days. Œstrone is more efficacious when given in repeated small doses than in one or two large doses.

Pain in the vulva due to a chronic inflammation or abnormally thin epithelium and kraurosis are also well treated by œstrone.

Vulvo-vaginitis of young children can usefully be treated by œstrogen. It may be given as stilbœstrol 1 mgm. each day or by small vaginal pessaries containing 5,000 units of œstrone on alternate days for a week. The exact duration of treatment must be adjusted to the resistance of the infection, and may be combined, if necessary, with daily instillations of 10% protargol.

A further use of this hormone is as a prophylactic given during the two weeks before an operation for prolapse in elderly women. In these patients the vagina is thin, congested and often mildly infected. The alteration of the mucosa during the preoperative fortnight is extraordinary and contributes to sounder healing of the tissues.

*Suppression of lactation* is quickly and completely produced by the œstrogens. Should it be necessary to prevent lactation for still birth or other reason, stilbœstrol in doses of 3 to 5 mgm. continued for five to six days after delivery will effectively prevent lactation. The breasts suffer little swelling or discomfort and there is no need to bind them tightly, give strong saline purges or restrict intake of fluid. It is well, however, to abstain from all animal protein during the first week.

After lactation has been established, a quicker result may be obtained by injection of an œstrogen in one of its commercial preparations up to a dose of 50,000 units or alternate days, for three doses. If there is any sign of recrudescence of lactation after the injections have ceased, it is enough to continue by giving stilbœstrol by mouth for a few days. Suppression of lactation by



the oestrogens is an advance on the old treatment by purging and restriction of food and fluid.

*Menopausal symptoms* are often greatly relieved by continued small doses of oestrogen. It may be given by mouth as stilboestrol or in a dose of 1,000 units of oestrone two or three times a week. The results are not uniform. Sometimes the flushes are controlled, and the nervous symptoms are also greatly improved, but in others there may be little effect. In our experience frequent small doses are of much greater benefit than an occasional large dose. Oestrone is perhaps more useful in improving the condition which follows bilateral oophorectomy, but here again the results are not always uniformly good.

*Amenorrhœa.* Endocrine products seem to be useful in primary amenorrhœa, but if the patient has developed amenorrhœa after having menstruated regularly, it is usual for menstruation to reappear if the true ovarian physiological sequence of oestradiol and progesterone is observed in treatment. The method is to give two large doses—say 50,000 units during the first week of treatment. During the following week nothing is given, after which, progesterone—2 rabbit units—is given three or four times during the next week. A further week of rest is followed again by repetition of injections of oestrone.

Secondary amenorrhœa springs from several causes, and it is necessary to select carefully the cases for ovarian therapy. It is stated (MacGregor) that 60% of all secondary cases follow some emotional disturbance, for which any therapy seems to be useless. In all cases menstruation sooner or later reappears spontaneously. In others the uterus is found to be much smaller than normal, and premature atrophy has taken place. Oestrogen and progesterone may succeed in a few of these patients, but as soon as treatment is discontinued, menstruation fails to appear. It is possible that adequate doses of the gonadotropic hormones might succeed, especially the luteinizing hormone, given alternately with oestrogen.

Those cases of amenorrhœa associated with anorexia nervosa should be treated on general medical and psychological lines.

Where amenorrhœa is a symptom of hypothyroidism of which the most obvious change is obesity, good results are quickly obtained by adequate doses of thyroid extract. Oestrogen and progesterone have proved of little value in the treatment of sterility. Where the pubescent uterus exists with other signs of structural hypoplasia, together with oligomenorrhœa and dys-

menorrhœa, it is tempting to employ œstrogen and progesterone. But results are disappointing. This type of case is probably due to defective ovulation, over which the end products of ovarian activity can have little or no influence. It is possible, however, that further trial of the serum gonadotropic (folliculising) hormone will prove successful.

*Induction of Labour.* A simple and reliable medicinal method of inducing labour would be a considerable advance on any surgical method. It is well known that so-called "medical induction" is unreliable for inducing labour, and comparatively useless for inducing premature labour. Posterior pituitary extract may produce a short series of contractions a few minutes after injection but they quickly disappear and labour is not induced. Some years ago Bourne and Burn demonstrated the synergistic effect of œstrogen and pitocin. After a small dose of œstrogen, the uterine muscle becomes sensitised to the effect of pitocin and hence much more responsive to its stimulus. On the findings of experiment, œstrogen should render "medical induction" much more reliable. Clinical experience is not yet in complete accord with experiment, but it is true that as the time of labour approaches, there will be a greater chance of induction by pituitary and castor oil being successful if preceded by an intra-muscular dose of 50,000 units of œstrogen. Earlier in pregnancy contractions can often be started by this technique, but they quickly cease and do not pass on to labour or abortion. Even during the last three weeks of pregnancy induction by 500,000 units of œstrone (as menformon) and pitocin has failed to provoke a contraction.

In addition to the foregoing conditions, œstrogen has been recommended for an immense number of others, for which subjective relief can often be claimed. But such cases are difficult to control and evaluate exactly.

### Indications for the Use of Progesterone

The normal function of this substance is to maintain the secretory phase of the endometrium. Until recently it has been difficult to obtain this hormone in sufficient dosage for clinical work, and its place was taken by using the urinary luteinising gonadotropic hormone, under the impression that it would cause luteinisation of the human ovary. No evidence has been brought forward that luteinisation occurs in the human subject, but, nevertheless, it has produced undoubted clinical results when it has been

used with discrimination. The synthetic product (progesterone) has greatly cheapened the original cost of treatment by corpus luteum.

*Habitual or Repeated Abortion.* Either progesterone or urine gonadotropic hormone (probably the latter is more valuable) have a remarkable effect in preventing abortion in women who have previously had a series of abortions for which no cause was known. The method of treatment is to give 100 units of gonadotropic hormone two or three times a week from the sixth week of pregnancy until the twenty-fourth week.

If progesterone is used, the dose should be 8 mgms. a week. For threatened abortion larger doses of Antuitrin-S or other proprietary preparation of prolan B may be given immediately, and in some cases the pregnancy may be saved. But as this favourable result often follows simple medical measures, it is difficult to appraise the value of this hormone therapy.

*Uterine hæmorrhages*—due to maintenance of the æstral endometrium—are sometimes successfully treated by progesterone or urine gonadotropic hormone. Such cases are those described as metropathia hæmorrhagica, in which the ovarian follicles fail to rupture and produce the corpus luteum. If the abdomen is opened during the period of hæmorrhage, corpora lutea cannot be found in the ovaries. Administration of urine gonadotropic hormone in large doses—say 500 units—is occasionally followed by arrest of bleeding. Similarly, some of the hæmorrhages of puberty and the menopause may be associated with unruptured follicles and absence of corpora lutea. These patients may also be treated on similar lines.

*Pre-eclamptic Toxæmia.* There have been varying reports on the value of progesterone in the treatment of toxæmia. Robson and Paterson, after some experiments on rabbits, treated twelve cases of acute toxæmia by 5 mgm. of progesterone a day. After three or four days' treatment all recovered, none had fits, and all cases showed gradual reduction of albuminuria and blood pressure.

On the other hand, James Young and many others consider progesterone useless in the treatment of acute toxæmia.

*Spasmodic Dysmenorrhœa.* If it is true that this form of menstrual pain is due to excessive or spastic contraction of the uterus, it is reasonable to expect that the inhibiting (luteinising) gonadotropic hormone would release the uterus from its spasm and so stop the pain. There are certain cases of this form of dysmenorrhœa that are undoubtedly relieved by giving 200 units

of antuitrin-S before and during the first day of menstruation. But it is necessary carefully to select the patients. The best results are obtained in those in whom the pain is severe for a few hours on the first day, with a scanty flow while the pain lasts. Those who have general pains before and during the whole of the "period" are not likely to be improved.

### TESTOSTERONE

Clinical experience of the use of the male hormone has given evidence of its value in the treatment of excessive menstruation and certain symptoms of the menopause (Abarbanel, Silberman and others). Abarbanel claims that testosterone causes a contraction of the myometrium whereby the arterial blood supply to the endometrium is reduced. He reports on a series of 30 cases between fifteen and forty-five years, showing various conditions of the endometrium. He used an initial dose of 10 to 25 mgm. of testosterone propionate intramuscularly, and this was repeated at intervals of two to four days. Relief of bleeding was obvious between one and four days. His instructions for prophylactic treatment are as follows: "If a secretory phase is found pre-menstrually, from 10 to 30 mgm. given in divided *subcutaneous* doses in the seven to ten days before the period will usually be sufficient to control the tendency to excessive flow. If hyperplasia exists, from 50 to 100 mgm. given in divided *subcutaneous* doses in the two or three weeks before the expected period will usually suffice.

Other methods of administration are by 10 mgm. tablets by mouth combined with bile salts, or the subcutaneous implantation of pellets of testosterone of 25 mgm. Abarbanel reports that in over 200 women treated by testosterone no case of masculinisation was noted.

Menopausal symptoms of flushes, sweats, paresthesia and loss of vigour have also been treated with success by testosterone in doses of 5 mgm. given two or three times a week according to severity, or by implantation of pellets of 25 mgm. It is probable that other gynaecological conditions will find relief by treatment with testosterone, but for the present, care must be observed in its administration either by too large or too prolonged dosage. The danger is the production of masculinisation, which has been observed by some gynaecologists. The urinary assay of the androgens is of value in diagnosis of adrenal tumours. Normally, the amount of androgen excreted in the urine is about 10 units a

day, but in the presence of adrenal tumours it may extend to 100 or 800 units a day.

### Serum Gonadotropic Hormone

The luteinising hormone has been described in an earlier section (p. 261). The serum hormone (folliculising) has not yet had sufficient clinical trial, but, in view of its stimulation of follicle-production, it may possibly prove of value in cases of sterility due to defective ovulation, and in cases where œstradiol production by the ovary is also deficient. The folliculising hormone is obtained from the serum of the pregnant mare at the fourth month of pregnancy, and the treatment should be by doses of 100 units twice weekly during the days from the first day to the twelfth day of the cycle.

### DANGERS OF HORMONE THERAPY

The sex hormones, in common with others already known, are not without danger if used indiscriminately. The association of the œstrogens with carcinogenic substances extracted from coal tar and the carcinomatous susceptibility of certain strains of mice when treated by œstrogen are examples of possible danger which might follow prolonged clinical administration of œstrogen to women, especially if for some reason, either local or familial, a carcinomatous diathesis is present. Gemmell and Jeffcoate have reported three cases of carcinoma of the cervix which followed comparatively small doses of œstrogen within a year. We know that the œstrogens cause hyperplasia of the endometrium, squamous metaplasia of a tissue which is normally columnar, and hypertrophy of the squamosa of the cervix. It is true that none of these conditions is malignant and may disappear after the administration of œstrogen is stopped. But these processes are those of growth and if they occur in a subject possessing other factors, *e.g.*, familial tendency or chronic irritation, concerned in the formation of carcinoma, œstrogen may be a dangerous substance.

Korenchersky and Hall have recently examined the effect of prolonged dosage of œstrogen and progesterone on rats. The results are in line with those of clinical work. An interesting detail is that the squamous metaplasia easily develops into leucoplakia which we know to be a pre-cancerous condition. That other factors are involved beside the influence of œstrogen is shown by the great variability in response of different rats

under the same doses of oestrogen. Some animals proved to be strongly resistant and showed no pathological change.

The hyperplastic effects caused by the oestrogens are also produced by testosterone but with continued administration they disappear and finally the uterus and ovaries undergo atrophy. The general result of observations both on animals and man is that the oestrogens are potentially dangerous, for example, when given for leucoplakia of the vulva and similar hypertrophic states of the endometrium which may appear at the menopause under the general description of "adenoma." It may be added that "cancer in the family" and an old traumatic lesion of the cervix might provide the conditions in which the trigger action of oestrogen would set off the process of which the end-result is carcinoma. Korenchensky and Hall also point out that no pathological changes follow prolonged administration of progesterone in female rats. If the doses are large enough they appear to be protective against metaplastic change of epithelium. It may be that in patients of the menopausal age oestrogens should always be combined with progesterone if given for more than a few doses. The dangers of testosterone will be evident after prolonged treatment or large doses. The tendency after initial hypertrophy will be to provoke atrophy, which is irremediable, and masculinisation. It is probable that both these ill-effects could be prevented by simultaneous treatment with progesterone.

A more likely harmful result following prolonged administration of oestrogen is inhibition of the production of gonadotropic hormones by the pituitary body. Cramer and Horning have described a condition closely resembling that following hypophysectomy, and Zondek reports the development of a pituitary tumour induced by prolonged administration of oestrogen, leading to dwarfing and atrophy of the genitalia.

A common, if minor, disturbance is a brisk uterine hæmorrhage a few days after cessation of the doses of oestrogen. It is not likely to be dangerous but may for the time cause alarm.

### ENDOCRINES AND VITAMINS

The relation of the endocrines to the metabolism of the vitamins is yet unknown, but it is possible that the two may be closely associated. For example, Collip reports that experiments on chickens show a relation between the specific metabolic factor of the pituitary and the metabolism of Vitamin A.

Writing on pituitary therapeutics, Collip says: "... in view of the fact that on the whole clinical experience with gonadotropic hormones has been somewhat disappointing, it appears to me that many new avenues of treatment with new types of pituitary extracts (e.g., the specific metabolic hormone) should be explored. It is possible that the present method of standardising gonadotropic extracts in terms of rat units may be misleading, and that clinical results may be obtained ... with specially prepared extracts which may be without visible effect on the ovaries of the normal rat. A clinical trial of standardised extracts of corticotropic and specific metabolic principles is now being undertaken and the results of these experiments may throw some further light on the etiology of certain types of menstrual disorder." (*Amer. Journ. of Obst. and Gynec.*, 1940, 39, 187.)

### EFFECT OF HYSTERECTOMY ON THE OVARY

A point of considerable clinical importance is how far hysterectomy is followed by atrophy or modification of function of the ovary. It is the custom of some operators to remove the ovaries in all cases of hysterectomy irrespective of whether or not there are any morbid changes in the ovaries. Others leave them *in situ* unless cysts, enlargement, œdema or other pathology is present. By the first it is claimed that the ovaries in any case will atrophy soon after the operation, that the menopausal symptoms will be easier after oophorectomy and that the danger of cystic growth will have been averted. The second maintain that, despite the removal of the uterus, the ovarian function persists for some time, the onset of the menopausal symptoms is more gradual and that the knowledge that she still possesses the ovaries intact is of real benefit to the patient's mental comfort. It is known that ovarian atrophy follows total hysterectomy within two years. The ovary will show before this time, a number of small unruptured follicles and no corpora lutea. Animal observations indicate that before the atrophy is complete, the follicular formation is irregular and cystic and corpora lutea are atypical and also cystic. The dependence of the ovary on the presence of the uterus suggests that there is an interaction between ovary and uterus as we see between ovary and pituitary and many other pairs of glands. Mishell and Molytoff (*Endocrinology*, 28, 8, 486) show that injection of an extract of endometrium (cow) into rabbits after hysterectomy retards the degenerative changes in the ovary. Further work in this direction might enable

successful treatment of the post-operative menopause by a hormone extracted from the endometrium rather than by stilboestrol or one of the oestrogens. We do not yet know enough of the action of hysterectomy on the ovaries at different ages to justify us in removing the ovaries in all cases. Towards the menopause it is either immaterial or even beneficial from the point of view of subsequent menopausal symptoms to remove the ovaries with the uterus. But for relatively young women where hysterectomy is necessary, it is probable that removal of the ovaries produces a more serious and sudden endocrine disturbance than would follow the natural ovarian atrophy a year or more after the operation.

While it is impossible to give in detail the references which have been consulted, we should like to acknowledge the work of Papanicolaou; Allen and Doisy; Allen, Pratt and Doisy; Parkes; Bramwell; Bellerby; Dodds; Whitehouse; Butenandt; Marrian; Evans and Long; Zondek; Zuckerman; Bishop, Cook and Hampson; Campbell, Lindrum and Sevringhaus; Wolfe; Korenchewski; Pratt, Pratt and Vaux; Loeser; Bartelmez; Jeffcoate; Robson and Paterson; J. Young; MacGregor; Cramer and Horning; Donald; Morgan and Davidson; Collip; Abarbanel; Gemmell.



## CHAPTER XIII

### OVARIAN TUMOURS

By WILFRED SHAW, M.D. (CANTAB.), F.R.C.S., F.R.C.O.G. ·

#### Classification of Ovarian Tumours.

No method of accurate classification of ovarian tumours has yet been devised, mainly because some of the rarer growths are of an indeterminate nature. Nevertheless, the following simple scheme groups the majority of the common forms with a fair degree of precision.

#### Epithelial Tumours

##### INNOCENT

- (a) Cystoma simplex.
- (b) Cystadenoma papillare.
- (c) Cystadenoma pseudomucinosum.

##### MALIGNANT

- (a) Primary.
- (b) Secondary.
  - (1) Typical.
  - (2) Krukenberg tumours.

#### Connective Tissue Tumours

##### INNOCENT

Fibromata.

##### MALIGNANT

Sarcomata.

#### Teratoid Tumours

- (a) Dermoid cysts.
- (b) Solid teratomata.

All the common forms of ovarian tumours are included in this system of classification, but there are certain notable omissions. First fimbrial cysts, which are regarded by Keith and others as being derived from ovarian remains in the outer part of the broad ligament, might perhaps be included. Indeed, it is not uncommon for papillomata to be found in the wall of fimbrial

cysts, and sometimes the cysts contain pseudomucin. Secondly, the chocolate cysts of the ovary are not included, but such cysts differ in many ways from neoplasms and should certainly not be regarded as having the same pathological significance as, for example, pseudomucinous tumours of the ovary. Chorion-epithelioma of the ovary can perhaps be regarded as a teratoid tumour, but when present in the ovary it always results from pregnancy and should therefore not be grouped in the same category as the bulk of the ovarian tumours. The rare tumours, such as the granulosa cell tumour, seminoma, arrhenoblastoma, struma ovarii, to which a good deal of attention has been paid in the last few years, cannot be grouped satisfactorily, but it should be remembered that such tumours are met with infrequently and are not of much clinical importance.

The incidence of tumours of the ovary is shown by the following results which were obtained from a study of 300 cases :—

	Cases.	Percentage.
<b>Epithelial Tumours</b>		
INNOCENT . . . . .		
(a) Cystoma simplex . . . . .	15	5.0
(b) Cystadenoma papillare . . . . .	26	8.67
(c) Cystadenoma pseudomucinosum . . . . .	91	30.3
MALIGNANT . . . . .	77	25.67
<b>Connective Tissue Tumours</b>		
INNOCENT		
Fibromata . . . . .	10	3.3
MALIGNANT		
Sarcoma . . . . .	4	1.3
TERATOID TUMOURS . . . . .	23	7.67
FIMBRIAL CYSTS . . . . .	16	5.3
CHOCOLATE CYSTS . . . . .	38	12.67

The incidence of the rarer tumours is approximately of the same order as the fibromata and were grouped as malignant epithelial tumours in the above classification.

The characters of the individual tumours are well known, but

it may perhaps be of service to emphasise the important features of each group.

### EPITHELIAL TUMOURS

**Cystoma Simplex.** This tumour is relatively rare and consists of a unilocular cyst lined by a single layer of ciliated epithelium. To the naked eye it may be mistaken for a distended Graafian follicle, but the characteristic epithelium in the wall enables the nature of the cystoma to be established without difficulty. The tumour is usually about 4 in. in diameter, but it does not necessarily replace the whole of the ovary, so that on occasion a cystoma can be resected and normal ovarian tissue left behind. The tumours have no particular age incidence and are bilateral in only about 6.6% of cases. They show a tendency to burrow between the layers of the broad ligament, when their removal may be technically difficult.

It is well known that pseudocystomata are sometimes found in the pelvis after patients have suffered from severe attacks of pelvic peritonitis, *e.g.*, following acute appendicitis. In these cases the wall of the pseudocystoma may consist of membranous adhesions, in part of the omentum, intestines and the ovary itself. Nevertheless, it is often possible at operation to dissect away remnants of the wall of the pseudocystoma, and histological examination shows the wall to have a structure similar to that of the typical cystoma simplex.

**Cystadenoma Serosum Papillare.** This tumour is undoubtedly related to the cystoma simplex, for its epithelium is ciliated and the contained fluid is similar to that found in serous cystomata. The essential feature of the tumour is the presence of papillomata in the cyst wall. The papillomata may take the form of flat, warty projections into the cavity, when histological examination shows them to be covered by inactive epithelium. This type of tumour is referred to as the stationary papillomatous form. In the second type, the papillomata are proliferating and may form villous projections into the cavity of the cyst. On occasion, richly arborescent projections are scattered, not only on the inner surface, but over the peritoneal surface of the tumour as well. Rarely, the papillomata are disseminated over the peritoneum and lead to the development of ascites. The proliferating forms of papillomata are covered with high, columnar epithelium which is ciliated and goblet cells are found intermingled with the columnar epithelium. In spite of the extreme pro-

liferation of the papillomata, there is reason to believe that the tumours become malignant only very rarely. Recent work goes to prove that an ovarian tumour is either innocent or malignant at the beginning of its development. Malignant degeneration in any type of ovarian cyst should be regarded as an infrequent complication.

*Clinically*, papillomatous cystadenomata of the serous type have no particular age incidence, but they show a well-marked tendency to be bilateral, bilateral tumours being found in about one-third of cases.

A rare type of tumour is recorded in which the surface papillomata become oedematous and vesicular and in which secondary vesicles are scattered over the omentum and peritoneum.

The explanation of the development of surface papillomata is very difficult, because there is often no evidence of rupture of the cyst wall. It has therefore been suggested that the surface epithelium of the ovary may undergo metaplasia to form surface papillomata. This explanation obtains some support from the serosal theory of the development of pelvic endometriosis.

*Cystadenoma Pseudomucinosum*. This tumour is the commonest of the ovarian neoplasms and is, of course, the familiar multilocular ovarian cyst containing pseudomucin. Mammoth tumours have been described weighing more than 200 lbs. The tumours are symptomless in the average case and the patient's attention is first directed to the abdominal enlargement. They arise most frequently between the ages of thirty and sixty, the incidence in each of the three decades being approximately equal. They are bilateral in only about 6% of cases, arising from the two ovaries in equal proportion. In spite of the enormous size the tumours may attain, they do not affect the menstrual functions. On the other hand, they sometimes cause post-menopausal bleeding.

*Morbid Anatomy and Histology*. The epithelium lining the loculi consists in the main of high, columnar epithelium with a cubical nucleus situated near the base of the cell, but another type of cell, ovoid in shape, with granular protoplasm, is found scattered amongst the high columnar cells. These cells are not found with all tumours, being present in only about 50% of cases. The epithelium is never ciliated, and in this way the tumour differs fundamentally from the cystoma simplex and the cystadenoma papillare. If the tumour is young, the loculi are small, but with old-standing tumours the septa between the loculi break down so that the end result is the formation of large

loculi, although there is invariably a small part of the tumour which consists of small loculi and which represents the actively growing part of the tumour. The loculi communicate eventually because the septum between adjacent loculi breaks down. Two methods can be distinguished. The more frequent is for the tissues of the septum to degenerate through impoverished blood supply. In the second method, the epithelial cells proliferate more actively than the connective tissues of the septum, and the epithelial cell layers give way under the pressure of the pseudomucin secretion contained in the loculi.

Pseudomucinous tumours sometimes burrow extraperitoneally, first between the layers of the broad ligament and finally they extend to the perinephric region. The ureter is usually displaced laterally and is found on the outer side of the tumour. In most cases it is necessary to remove the uterus as well as the tumour because of the intimate relations of the cyst to the uterine vessels.

Infection of pseudomucinous tumours is met with as a complication of gonococcal and puerperal salpingitis. The tumour may also be infected as the result of torsion, when adhesions to the intestine allow micro-organisms to pass from the bowel to the tumour. Rarely the tumour may be infected from such suppurating conditions as appendicitis, diverticulitis and peritonitis. At the present day, infection is a relatively rare complication of ovarian tumours, far less frequent than in the days before the operation of ovariectomy was introduced. If one reads the medical literature of the early nineteenth century, one appreciates how frequently ovarian tumours became infected. If ovarian tumours remain untreated, some time or other they might be infected by way of the blood stream. Such cases must be very rare in modern gynaecology.

**Papillomatous Forms of Pseudomucinous Cystadenoma.** It is well established at the present day that there is a type of tumour which is intermediate in form between the papillary serous cystadenoma and the pseudomucinous cystadenoma. The tumours are not uncommon and are of great theoretical interest, for their structure suggests that pseudomucinous tumours and serous cystadenomata have a common origin. These tumours contain actively growing papillomata and are seen most frequently in women of post-menopausal age. They are multilocular and the lining cells are high columnar in type. There is another type of tumour which is rather similar pathologically, although it arises in younger women, when the tumour consists of a series of

spherical loculi each about 1 in. in diameter, containing papillomata, while the connective tissue stroma is infiltrated with pseudolutein cells.

**Rupture of Pseudomucinous Tumours.** Rupture by direct violence is a rare complication and depends upon either violent trauma to the abdomen, or pressure by the foetal head in childbirth, when the tumour lies in Douglas's pouch in advance of the presenting part. The majority of cases result from spontaneous rupture, which depends upon the epithelial elements of the tumour outstripping the connective tissues in their rate of growth. In such cases, there may be no clinical signs of any kind. Rupture of malignant tumours depends, of course, upon infiltration and erosion of the cyst wall by the malignant cells.

**Pseudomyxoma of the Peritoneum.** It does not follow that pseudomyxoma of the peritoneum invariably follows spontaneous rupture of an innocent pseudomucinous tumour. In the condition pseudomyxoma of the peritoneum other factors are at work. For example, there is often an association with a mucocoele of the appendix, or with a carcinoma of the large intestine. Admirable reviews of the literature are found in the articles of Wilson (2) and Krivsky (3). In pseudomyxoma of the peritoneum the omentum is studded with small tubercles of actively growing, high columnar epithelium, which secrete pseudomucin into the peritoneal cavity. Incidentally the condition is three times as common in men as in women.

The condition, pseudomyxoma of the ovary, is extremely rare, but is comparable to pseudomyxoma of the peritoneum, except that the pseudomucinous material is restricted to the neighbourhood of the ovary. The ovarian tumour is a papillomatous pseudomucinous cystadenoma in which the papillomata are also scattered over the peritoneal surface of the tumour.

### Ovarian Carcinomata

Malignant ovarian tumours comprise approximately one-fourth of all neoplastic tumours of the ovary. This means that one in four of every ovarian tumour operated upon is malignant. It is well known that secondary or metastatic carcinomata of the ovary are common, the tumours arising particularly from primary growths of the stomach, large intestine and rectum, the body of the uterus, the breast, the thyroid and the gall-bladder. The incidence of these metastatic tumours is particularly high in post-mortem material, but with the clinical material seen by

gynæcologists approximately 20% only are secondary in type. Four-fifths of the malignant tumours of the ovary seen in clinical gynæcology are primary growths of the ovary itself.

**CLASSIFICATION.** The classification of primary malignant ovarian tumours offers a problem of exceptional difficulty, and no satisfactory classification seems possible at the present day. The first question to be answered is the frequency with which innocent ovarian cysts become malignant, for the question is clearly of great clinical importance. In the first place, it is very rare indeed for a large pseudomucinous tumour to become malignant. Only about 6% of pseudomucinous tumours show malignant degeneration, and quite often it is impossible to decide in such cases whether the tumour was malignant or not at the beginning of its development. Serous cystomata are not proliferating in type and consequently never show a tendency to malignant change. The difficult cases are the papillary serous cystadenomata of the proliferating type, for these tumours often contain richly arborescent papillomata, sometimes diffused over the peritoneal cavity. Nevertheless, it is very rare for such tumours to show malignant change in spite of the fact that the papillomata may be disseminated over the peritonæum. Mistakes are made because some ovarian carcinomata are papillomatous in type and superficially resemble these innocent cystadenomata.

In any classification of primary ovarian carcinomata it is best perhaps to pay less attention to the malignant tumours which arise from pre-existing innocent ovarian cysts than to the more common primary malignant tumours. The following system of classification has been suggested.

**GROUP I.** Tumours which are papillomatous in type :—

(a) *Psammocarcinoma*. These tumours represent papillary serous cystadenomata which have become malignant.

(b) *Malignant Serous Papillomatous Tumours*. These tumours, usually unilocular, contain serous fluid and coarse, friable malignant papillomata.

These tumours superficially resemble the innocent papillomatous tumours, but they differ in their histology.

**GROUP II.** *Malignant Pseudomucinous Tumours*.

These tumours superficially resemble small innocent tumours, but the epithelium lining the loculi is frankly malignant.

**GROUP III.** *Solid Carcinomata*.

The tumours in this group are the most difficult to interpret.

They are of high malignancy, and, although in the main they retain a resemblance to pseudomucinous tumours, the activity of the epithelium obliterates any tendency to the formation of loculi. The rare tumours of the ovary, *e.g.* seminoma, etc., are usually included in this group, but it will be shown later that the rare tumours are usually innocent in type.

**Metastatic Carcinoma of the Ovary.** Metastatic tumours of the ovary which are secondary to carcinoma of other organs of the body are met with frequently in autopsy material. Statistics show that about 20% of ovarian tumours, which can be diagnosed clinically as malignant, are secondary growths from primary growths of other organs. This incidence is important because the prognosis with such tumours must necessarily be hopeless.

It is customary to classify these metastatic ovarian tumours into the typical tumours, which correspond histologically with the primary growth, and Krukenberg tumours, which differ fundamentally in their history.

**Krukenberg Tumours.** This tumour was described by Krukenberg (4) in 1896 as a mixed tumour of the nature of both a sarcoma and a carcinoma. The tumours are bilateral, about 4 in. in diameter, freely movable, with smooth, bossed surfaces. The consistence is waxy, but sometimes small, cystic spaces due to degeneration of the growth are found. The tumour consists of a fibrosarcomatous stroma in which lie the characteristic signet-ring cells. The cells are large, measuring about 0.008 mm. in diameter, and possess a granular cytoplasm. Sometimes the signet-ring cells are scattered loosely in the stroma. At other times they are bunched together and may show a true alveolar arrangement. The tumours are now regarded as secondary growths in the ovary, arising from primary growths in the stomach, large intestine or gall-bladder. The importance of the tumours apart from their peculiar histology, is that they may be regarded as innocent tumours at operation, because of their free mobility, and, as they are easily removed, a favourable prognosis may be given. Quite frequently the primary growth is small and hardly palpable and may not be discovered at operation.

The pathology of Krukenberg tumours is of very great interest because it has been shown that the ovaries are involved by lymphatic permeation by retrograde spread along the ovarian lymphatics from the superior gastric group of lymphatic glands. The tumours are certainly not caused by implantation of malignant cells upon the cortex of the ovary. The peculiar shape of the



signet-ring cells is perhaps determined by the fact that the cells involve the ovaries, either singly or in small bunches, and that the reaction of the stroma of the ovary compresses and distorts them.

Krukenberg tumours are relatively uncommon. The ovarian metastases which are usually seen are irregular, nodular tumours, associated with multiple metastases disseminated over the peritoneum and omentum. Even so, the growths in the ovary are always much larger than other metastases, so that it must be assumed that the ovary presents an excellent medium for the growth of malignant cells. There is reason to believe that lymphatic permeation is often combined with peritoneal implantation in the process of development of such tumours.

**Coincident Tumours of the Uterus and Ovary.** The association of carcinoma of the body of the uterus with carcinoma of the ovaries is well known. In some cases, the ovarian tumours are secondary deposits from the primary growth of the endometrium, metastasis occurring by lymphatic permeation. Similarly, carcinoma of the ovary sometimes produces a metastasis in the uterus just as, on occasion, metastases are found in the vagina from such primary growths. There is, however, a third type of case in which carcinoma of the ovary arises coincidentally and independently of the primary growth in the body of the uterus. The tumours are of academic interest, for they illustrate how malignant disease may, on occasion, be multicentric. The tumours are usually quite different in their histology.

### **Metastasis of Primary Ovarian Carcinomata**

The commonest metastasis of a malignant ovarian tumour is the papillomatous growth of the peritoneum, which is found particularly in the pouch of Douglas, on the posterior surface of the uterus and on the omentum. In most cases the malignant cells erode through the capsule of the primary growth in the ovary and become disseminated over the peritoneum. Peritoneal metastases are formed partly by implantation, but also through invasion of the lymphatics which open directly into the peritoneal cavity. In this latter process, the malignant cells invade the sub-peritoneal lymphatics and produce nodular growths. The peritoneal implantations are found in 60% of cases of malignant ovarian tumours which are operated upon. They are responsible for the development of ascites. The peritoneal metastases are

always well marked in the omentum, and this distribution is explained by the known process by which particles of inanimate material are rapidly taken up by the omentum after injection into the peritoneal cavity. It has been shown experimentally that malignant cells are taken up in the same way, so that if an animal is killed a few weeks after intraperitoneal injection large omental deposits will have developed.

Malignant ovarian tumours spread directly into the mesovarium, into the broad ligament, along the Fallopian tube and to adjacent intestine and omentum.

Spread by way of lymphatics is usually overshadowed by the formation of intraperitoneal deposits, but involvement of the pre-aortic group of lymphatic glands can be demonstrated in post-mortem material. On rare occasions the malignant cells may permeate to the mediastinal lymphatic glands and by ulceration into the pleura may cause pleuritic effusion. Very rarely a malignant gland can be demonstrated in the left supra-clavicular region.

Spread by way of the blood-stream is seen from time to time in the case of malignant tumours arising in young women. The metastases which are found in the vaginal wall have already been mentioned and are believed to develop by retrograde spread along either the lymphatics or the venous channels which lie along the course of the vagina.

### Clinical Features of Malignant Ovarian Tumours

The majority of malignant ovarian tumours arise between the ages of fifty and sixty. Less than 25% of cases are seen with patients younger than forty-five. At least 60% of malignant ovarian tumours arise in patients past menopausal age.

In women of the child-bearing period of life, bilateral malignant tumours may cause amenorrhœa, but this symptom is uncommon. In patients of post-menopausal age, the tumours may cause uterine hæmorrhage. The relation of post-menopausal hæmorrhage to ovarian tumours will be discussed later. The two symptoms which bring patients to seek medical advice are abdominal pain and abdominal swelling. The pain is usually fairly severe, much more severe than with innocent tumours. The abdominal swelling is often due to ascites.

**DIAGNOSIS.** The signs of malignancy with ovarian tumours may perhaps be emphasised. First is the presence of ascites, but statistics show that demonstrable ascites can be detected clinically



that such female connective tissue cells suddenly start to develop to form the granulosa cell tumours and, as the cells are feminine in type, they secrete œstrin, which may produce post-menopausal uterine hæmorrhage.

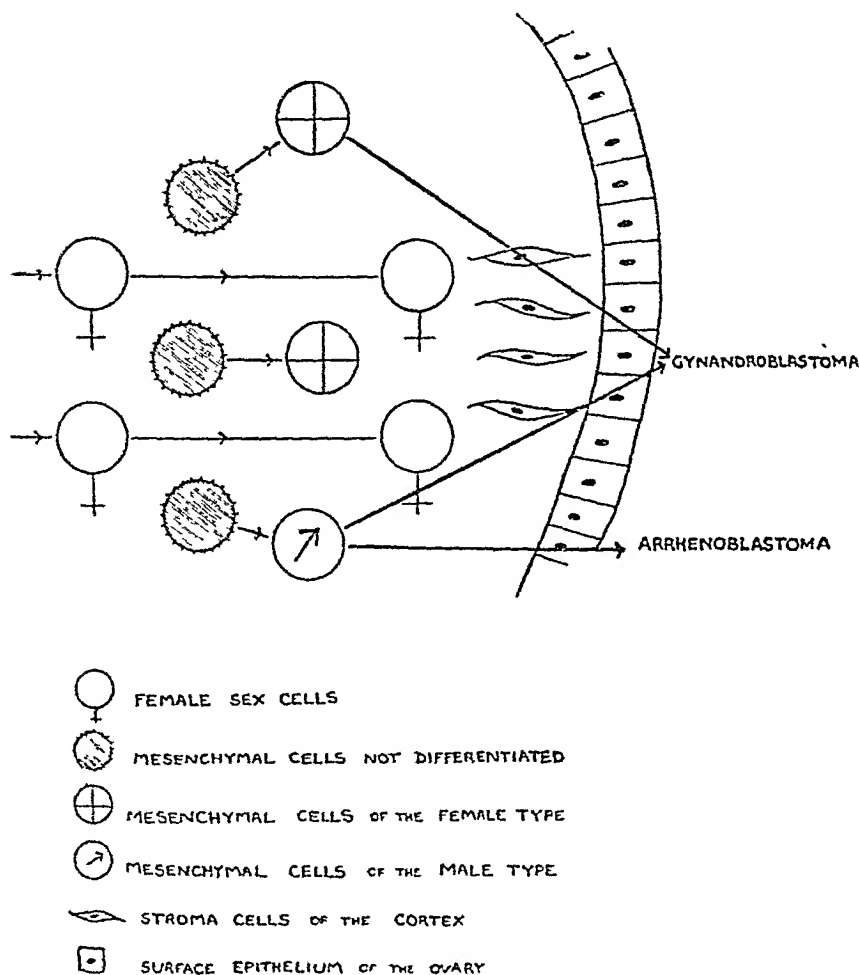


FIG. 60. Scheme to show the development of virilising Ovarian Tumours.

The second possibility is that mesenchymal cells, which are anterior in time to the invasion of the genital ridge by the sex cells, may start to develop into a tumour. If the cells are undifferentiated sexually, the resultant tumour is a seminoma or dysgerminoma. The tumour is non-sexual in type and has no hormonal influence. The tumours have long been known in the testes

and have been destroyed in the ovary by French authors who have called them seminomata. There seems to be no point in following the German school and using the term dysgerminoma (Fig. 63).

Arrhenoblastomata are believed to be produced from a primitive ovo-testis. In the first years of life the patient is typically feminine, but the dormant testicular elements subsequently grow to form a testicular tumour with virilising properties. The tumours never contain spermatogonia and are believed to be mesenchymal in origin (Fig. 60). These rare tumours will be considered in detail subsequently.

The origin of the common epithelial tumours of the ovary, curiously enough, seems to be much more obscure than that of the rare tumours named above. There is no doubt that down-growths from the surface epithelium of the adult ovary are commonly seen in sections of the ovary and quite frequently small cystic spaces are formed when the mouths of these depressions are shut off from the peritoneum. Moreover, the epithelial lining is ciliated, so that the small cystic space is exactly similar to a small cystoma simplex, except that small cystomata are always surrounded by a small capsule of fibrous tissue. Moreover, a small papillary cystadenoma has been described in the ovary which almost certainly originated in the same way. The evidence for the origin of these serous tumours by this process is very strong, but, quite obviously, the theory explains only from what structure the tumour arises: it offers no suggestion of the stimulus which causes the invaginations to occur.

The origin of pseudomucinous cystadenomata and of teratoid tumours is unexplained at the present day. It is almost certain that the tumours must be related in some way, because they are found so frequently combined. On the other hand, although the idea that the tumours arise from the ovum is superficially attractive, there are many serious objections to this theory. For example, a dermoid cyst never shows signs of trophoblastic tissues. It is difficult to believe, therefore, that a teratoid cyst can possibly arise directly from a normal ovum. It is possible, however, to explain the origin of a dermoid cyst in some such way as the following. If an ovum divides and subdivides until the inner cell has become differentiated, if we suppose that some of the cells of the inner cell mass persist while the rest of the cells of the dividing ovum degenerate, it is possible to account for the appearances of a dermoid cyst. Moreover, with a little ingenuity it is possible to explain pseudomucinous cystadenomata

as developing from some primitive epithelium of the embryo proper, *e.g.*, an allantoic duct. There is, of course, no direct evidence to support this theory, but the theory does account for most of the known facts of the structure of these tumours. Again, the Brenner tumour, which is found so frequently in association with pseudomucinous cystadenomata, can be explained, for the transitional epithelium of which it is composed is easily accounted for along these lines. There is no objection to postulating such an abnormal division of an ovum if one considers the extraordinary processes of degeneration and regeneration which happen to the ova during intra-uterine life. The old ideas of the derivation of dermoid cysts from Graafian follicles have been discarded at the present day. Wilm's blastomere theory and the idea of parthenogenesis are both introduced into the theory which I have put forward above. Obviously the extra-ovarian teratoid tumours can be explained along the usual lines of ovarian remains being left in the lumbar region as the ovary descends into the pelvis. The curious dermoid cysts which are found in other parts of the body can be explained by supposing that the primitive sex cells migrate from the mesenteric region and pass to other parts of the body instead of passing to the ovary. The one link with the chain of evidence which is unsatisfactory is the papillary cystadenoma which is partially pseudomucinous and partially serous in type.

### The Bilateral Tendency of Ovarian Tumours

Ovarian tumours show a remarkable tendency to be bilateral as illustrated by the following table :—

	Number of cases.	Bilateral.	Percentage.
Chocolate cysts . . . . .	38	13	34.2
Cystoma simplex . . . . .	15	1	6.6
Cystadenoma serosum papillare . . . . .	26	9	34.6
Carcinoma :			
Primary . . . . .	46	33	71.0
Secondary . . . . .	7	7	100.0
Fibromata . . . . .	10	1	10.0
Sarcoma and endotheliomata . . . . .	4	3	75.0
Dermoid cysts . . . . .	22	4	18.2
Solid teratoma . . . . .	1	0	0.0
Fimbrial cysts . . . . .	16	1	6.25

These statistics show that malignant tumours are bilateral in 76·7 cases, while of 219 innocent cases the tumours were bilateral in 16·0%. This means that if bilateral ovarian tumours are found at operation, the chances are about five to one in favour of the tumours being malignant. The frequency with which ovarian tumours are bilateral is of great theoretical interest, for the relatively high incidence of bilateral innocent tumours suggests that the stimulus to tumour formation affects both ovaries simultaneously. There is no reason to believe, with innocent tumours, that one ovary is directly affected from the growth of the opposite side. Again, with malignant ovarian tumours there is often little reason to suppose that one ovary is affected by the spread of malignant cells from the opposite side. In most cases of primary malignant ovarian tumours, the malignant growth develops simultaneously in each ovary. Histological investigation of early cases of primary malignant ovarian tumours strongly supports this view.

### Granulosa Cell Tumours

These tumours have been investigated very thoroughly during the last few years (6). There is still, however, a great deal of confusion as to which ovarian tumours should be grouped under this heading, and this confusion is illustrated in quite recent publications. The tumours consist of cells which are almost identical with the granulosa cells which line ripening Graafian follicles; indeed the most characteristic feature of the tumours is the almost exact resemblance of the constituent cells to granulosa cells. It is important at this stage to emphasise that the tumours never contain objects which can be supposed to be ova. In this way the tumours can be distinguished from Brenner tumours, and it is clear from the term oöphoroma ought never to be used for granulosa cell tumours. With almost all granulosa cell tumours, at some part or other, the tumour cells merge with the normal stroma cells of the ovary so that it is impossible to distinguish the line of demarcation between the tumour cells and the cortical stroma. The cells of which the tumour is composed always stain deeply with hæmatoxylin, and in the early stages of development the cells are arranged in columns. Even then bands of hyaline tissue can be identified between the columns of cells, and the hyaline tissue is exactly comparable to that found in atretic follicles. Next, small Call-Exner bodies can usually be distinguished in some part or other of the tumour. These characteristics

—the essential features of the tumour—can be summarised as follows :—

- (1) Cubical cells, staining deeply with hæmatoxylin.
- (2) Arrangement of the cells into columns, cords, or trabeculæ.
- (3) Hyaline tissue intervening between the trabeculæ.
- (4) Presence of Call-Exner bodies.

In addition, the tumours usually secrete the hormone œstrin and the action of the hormone on the endometrium of post-menopausal women by reducing œstrogenic proliferation induces post-menopausal hæmorrhage.

These simple characters have been emphasised to show how the granulosa cell tumours should be defined. The histology of some granulosa cell tumours is, however, much more difficult than this, because in mature growths the cells may become epithelial in type and small spaces, full of fluid, roughly comparable to a Graafian follicle, may become differentiated. It is justifiable to call this form of tumour a folliculoma. It is perhaps best to divide the innocent granulosa cell tumours into three types :—

- (a) An early undifferentiated form consisting of a solid tumour composed of granulosa cells without differentiation into trabeculæ.
- (b) The trabecular form.
- (c) The folliculoma form

Some granulosa cell tumours are malignant in type and may be presumed to be derived from the folliculoma form. The rarity of malignant granulosa cell tumours must, however, be emphasised. The metastases are extremely interesting, the opposite ovary first becomes involved, then metastases form in the lumbar region. Metastases have been described in the mesentery, the liver and the mediastinum. The metastases retain the hormonal influence of the primary growth, so that the patient develops uterine bleeding after the original tumour has been removed.

It is well known that granulosa cell tumours produce post-menopausal hæmorrhage. The uterus usually shows a moderate degree of myohyperplasia. The endometrium is thickened and congested and there may be small protrusions from the endometrium. Cystic glandular hyperplasia is present to some degree in post-menopausal cases, but it is well known that some degree of cystic change is commonly found in the glands of the endometrium after the menopause. The hæmorrhage is not induced by necrosis such as occurs during menstruation or in metropathia hæmorrhagica.

**MORBID ANATOMY.** The tumours rarely exceed 4 in. in diameter



and mostly take the form of lobulated swellings of soft, rather friable material, grey in colour. The cut surface is reticulate and, characteristically, there is always some degree of interstitial hæmorrhage. Indeed, these peculiar hæmorrhages often enable the true nature of the tumour to be diagnosed by naked-eye examination.

### Clinical Aspects of Granulosa Cell Tumours

The tumours are most common between the ages of forty and fifty. When they arise in women of post-menopausal age they produce post-menopausal hæmorrhage. The tumours have been described in younger patients and even in children before puberty. When the tumours arise during the child-bearing period of life they often cause amenorrhœa for three or four months, which is followed by continuous bleeding which leads the patient to seek medical advice. The tumours are suspected clinically because of the disturbance they produce in the menstrual functions. In elderly patients the uterus should be curetted to exclude a coincident carcinoma of the body. The tumours themselves, apart from their endocrine influences, behave in the same manner as the more common ovarian tumours.

The treatment is of necessity surgical and in post-menopausal patients should consist of removal of the uterus as well as the appendages. In patients of the child-bearing period of life the tumour alone should be removed. It seems to be well established with malignant granulosa cell tumours that the prognosis is not necessarily bad, for the tumours are radio-sensitive and in any case the development of metastases is a late phenomena.

### The Rare Ovarian Tumours

**Arrhenoblastomata.** These tumours are extremely rare, not more than two or three having been described in Great Britain. Microscopically the tumour consists of columns of cells arranged in the form of trabeculæ. If these columns are cut across, an appearance is produced not unlike that of the collecting tubules of the kidney. In other ways the tumour resembles superficially a granulosa cell tumour, except that the cells are more stellate, with larger nuclei and less protoplasm. The tumours are relatively small and are usually polycystic. They are almost always innocent in type.

The interest of the tumour is two-fold. First, it is of great clinical importance in that it is virilising, so that the individual develops well-marked masculine characters. The patient has

amenorrhœa, hair develops on the lips and chin and on the body. The breasts become small and the deposition of fat around the breasts and hips, so characteristic of the female, disappears. The clitoris hypertrophies although a large penis is never produced. The tumours are unilateral and arise in women younger than thirty. Secondly, it has been pointed out already that the tumours are believed to arise from a primitive ovo-testis, the testicular part being dormant until the tumour starts its development.

**Seminoma or Dysgerminoma.** These tumours are not uncommon and frequently become as much as 12 in. in diameter. They form solid tumours, pale in colour, with a smooth surface, and the consistence is smooth and friable. The tumour consists of large cells, rich in protoplasm, with spherical nuclei which are very characteristic (7). The cells are arranged either in bunches or in small alveoli. It is important to realise that this alveolar form is not necessarily malignant. Giant cells are nearly always found in the tumours and the connective tissue septa between the alveoli are usually infiltrated with lymphocytes.

The tumours almost always arise before the age of twenty and are frequently bilateral. Recently Stabler and Greig Thompson (8) (9) have recorded a case of a seminoma obstructing labour. The tumour exerts no hormonal influence; it has no virilising properties at all, nor does it disturb the menstrual functions. On the other hand, the genitalia of patients suffering from seminoma of the ovary are often infantile in type.

The interest of the tumour depends first upon its resemblance to the seminoma of the testis, secondly upon its benign nature in the average case although histologically it may seem to be malignant, and, thirdly, upon its ætiology. The explanation of the ætiology of the tumour which is accepted at the present day is that it arises from cells which correspond to the mesenchymal cells of the genital ridge prior to the invasion of the primitive sex glands. Such cells are undifferentiated sexually into either male or female types. It is appreciated at the present day that many of the cases described as sarcoma of the ovary in women were seminomata. Although the tumours are referred to as dysgerminomata by the German school, they were described originally by French authors who appreciated their identity with the testicular tumours and who used the term seminomata.

**Gynandroblastoma.** This tumour is extremely rare and combines the characteristics of both the granulosa cell tumour and the arrhenoblastoma. Histologically, the tumour consists of the

typical tubules of an arrhenoblastoma, combined with trabeculae of granulosa cells. The interest of the tumour is that the patient develops masculine characteristics, although these virilising effects are not so well marked as with arrhenoblastomata. The tumour may be explained theoretically on the assumption of its derivation from a primitive ovo-testis, so that both male and female constituents simultaneously develop to form tumours. A case has been recorded by Plate (10).

**The Brenner Tumour.** This tumour, described originally in 1907 as an oöphoroma, has been responsible for much of the confusion which existed until recently about ovarian tumours which were reputed to contain ova. The tumour consists of cords of transitional or squamous epithelium. In the middle of the cord lie droplets of secretion which stain fairly deeply with eosin. If such a cord of cells is cut through transversely, the appearance is not unlike that of a young Graafian follicle. It was because this appearance was mistaken for that of a follicle that the term oöphoroma was introduced. At the present day it is appreciated that Brenner tumours having nothing whatsoever to do with either Graafian follicles or ova. The tumours are very frequently associated with pseudomucinous cystadenomata when they form small nodules in the wall. In some cases the cords of cells contain cells which are high-columnar in type, and often it is easy to trace the transition between Brenner tumour and the pseudomucinous cystadenoma. The exact aetiology of the Brenner tumours is unknown. Schiller (11) maintains that the tumour is derived from the remains of the urinary system, which get caught up in the genital system during its development. Schiller's view, though ingenious, offers no explanation of the association between the tumour, pseudomucinous cystadenoma and the dermoid. It seems much more likely that the Brenner tumour is fundamentally of the same nature as these tumours and, as has already been pointed out (see p. 293), it is possible to offer some explanation of this association. It should be remembered that in the typical clinical case of Brenner tumour, the patient is of post-menopausal age and the tumour forms a swelling about  $1\frac{1}{2}$  in. in diameter. Some of the patients complain of uterine bleeding, but it must be emphasised that Brenner tumours, as a general rule, exert no hormonal influence. It should be remembered again that other tumours than granulosa cell tumours may cause post-menopausal hæmorrhage.

**Struma Ovarii.** These tumours are very uncommon. They

consist almost entirely of thyroid tissue and must be clearly distinguished from dermoid cysts which contain areas of thyroid tissue in the wall. A struma of the ovary may be a solid tumour, resembling almost exactly the naked-eye appearance of colloid goitre. The secretion stains with iodine and the histology of the tumour is similar to that of a colloid goitre. The epithelium lining these vesicles is, however, usually cubical and it may be flattened. Cases have been recorded when an ovarian struma has produced signs of thyrotoxicosis. The struma tumours have been confused with the follicular form of granulosa cell tumour and even with pseudomucinous cystadenoma. They are almost certainly teratoid in origin and can be explained along the lines which have already been indicated for pseudomucinous cyst adenomata. One of the recorded cases is interesting because the patient's mother developed a granulosa cell tumour.

**Xanthofibroma Thecacellulare.** This tumour, which has been described only recently, takes the form of a solid ovarian tumour up to about 3 in. in diameter. The tumour is yellowish on section and histologically it consists of cells which resemble the theca interna cells of Graafian follicles. The yellow colour is produced by droplets of lipoid, contained both in the protoplasm of the cells and also in the intercellular spaces. The tumours are intensely oestrogenic, so that they cause post-menopausal hæmorrhage and are also responsible for amenorrhœa in young girls. A case was admirably reported by Patterson and McCullagh (12). The tumours obviously arise from the cells of the cortical stroma of the ovary. They can be explained theoretically by assuming that the stroma cells revert back to theca interna cells which proliferate to form a tumour—another example of the theory put forward in this chapter to explain the origin of ovarian tumours.

### Complications of Ovarian Tumours

The complications of infection, impaction and rupture are well known and require no comment. Malignant change has been dealt with in the section on Malignant Ovarian Tumours. Curiously enough, there is no explanation of torsion which is generally accepted at the present moment. The plea may perhaps be made that the theory put forward by the writer some years ago should receive a little more attention. The theory supposes that the most important factor in producing torsion is the pulsation of the arteries in the pedicle. On general principles, it is most likely that the mechanism of torsion of such different structures

In one of the cases of pseudomucinous cystadenoma, the hæmorrhage was proved to be due to a coincident carcinoma of the body of the uterus. This relation is of some clinical importance. The interesting feature of the analysis is the frequency with which these innocent tumours may cause uterine hæmorrhage. There was no relation to torsion of the tumour and mechanical causes of bleeding were examined and excluded. It is most likely that in all cases the uterine bleeding was œstrogenic caused by the production of œstrin in the ovarian tumours. It should be emphasised again that post-menopausal bleeding in the presence of an ovarian tumour does not necessarily mean that the tumour is granulosa celled. Also, of the other rare ovarian tumours, the only one which is known to produce post-menopausal bleeding is the Brenner tumour, and this tumour is not necessarily œstrogenic.

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## CHAPTER XIV

# RADIOLOGICAL INVESTIGATION AND DIAGNOSIS IN GYNÆCOLOGY

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### Introduction

In gynæcological practice, the value of plain or simple radiography is limited. Radiography with contrast media, however, can be of great value. The contrast media may be opaque, *e.g.*, the iodised oils such as lipiodol, or non-opaque such as any non-toxic gas. The two methods used are, firstly, *pneumoperitoneum* with gas injection either *via* the Fallopian tubes or through the abdominal wall (paracentesis), and secondly *utero-salpingography*, using opaque media.

Occasionally, useful information is afforded by such investigations as a barium enema, or excretion or instrumental urography, to help in differential diagnosis or to show the relationships of the colon, bladder and ureters to the female generative organs. Valuable studies of sinus tracts and fistulæ may be made by screen-controlled lipiodal injections.

The radiological examination of the appendix may be helpful in the differentiation of chronic tubal and appendicular lesions.

The value of radiography of the lower vertebral column and the bony pelvis in investigating low back pain needs no further support in this chapter.

**Plain Radiography.** The limitation of the value of plain radiography is due to the fact that in normal states and in most pathological conditions the female generative organs have the same radiographic density as the surrounding structures and cannot therefore be appreciated by contrast.

The recognition of lesions by plain radiography is dependent on (i) the demonstration of large soft tissue masses which are appreciated usually by their marginal outlining from gas in dis-

placed intestines, and (ii) the presence of calcium deposition. The two conditions most commonly seen are calcified fibroids and ovarian dermoid cysts.

Calcified fibroids are seen as rounded or oval irregularly calcified masses resembling an opacified sponge; there is a tendency for the peripheral margins to be more regular than the central zone.

**Ovarian Dermoid Cysts.** Calcification or ossification has been reported by different authors as occurring in from 18 to 49 per cent. of ovarian dermoids. When tooth formation is present in a cyst, the recognition is usually easy; sometimes one or more teeth may be perfectly developed. The size of the bony or dental opacity gives no clue as to the size of the cyst, which may be considerable. Sometimes ovarian dermoid cysts undergo mural calcification and will be seen as large rounded or oval calcific ring shadows.

Even when no calcification is present in a dermoid, such a lesion may be recognised because of the relative translucency of the sebaceous material within the cyst. Robins and White (1) have described the following appearances: a persistent round or oval translucent shadow is seen within the pelvis, showing some mottling and surrounded by a more opaque peripheral ring demarcating the neighbouring strictures from the translucent area. The translucency is due to the sebaceous fluid material, the mottling to the hair content and the peripheral ring to the solid cyst wall.

Other gynaecological causes of calcification are less common; calcification may sometimes be seen in the walls of other ovarian cysts but seldom in such an amount as to allow recognition. In a chronic tuberculous pyosalpinx, calcific debris may be seen as a partly granular, partly smeary opacity of varying density.

It is perhaps not out of place to mention briefly the "non-gynaecological" causes of opacities in the pelvis which may be seen in radiographs. Faecal material in the pelvic colon and rectum is often observed when it is surrounded by gas in the gut but particularly when it contains unabsorbed opaque medicinal substances, *e.g.*, bismuth preparations. Arterial vascular calcification is common in elderly and diabetic subjects. Calcified lymph nodes are commonly observed in groups or singly, especially in the right sacro-iliac zone. *Phleboliths* are common and are usually multiple; they appear as small rounded opacities often arranged in linear grouping near the side walls of the pelvis and in the parametrial zones in parous women.



FIG. 61. Calcified fibroid.



FIG. 62. Teeth in a dermoid cyst.

[To face page 304.]





FIG. 63 Utero-salpingography, right, normal tube and average "spill", left, long and tortuous tube

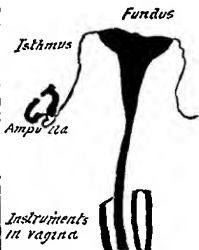


FIG. 64. Normal uterus and tube just before "spill."

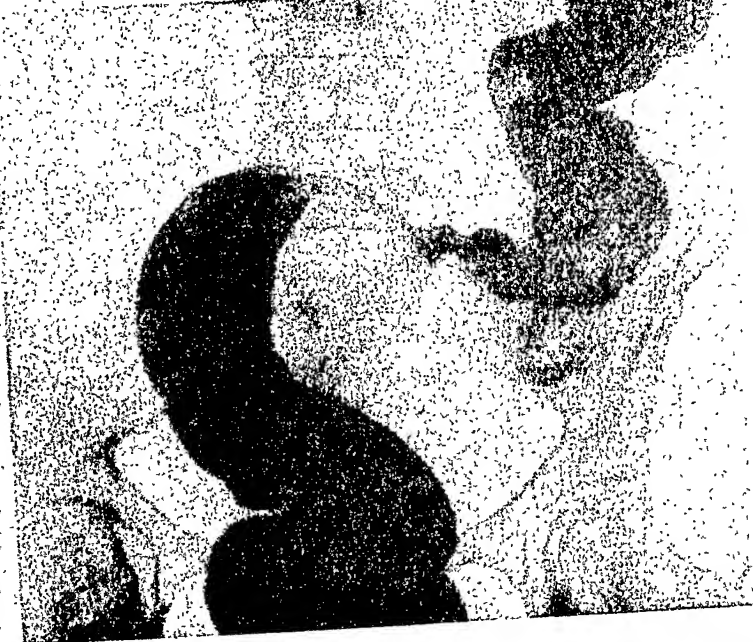


FIG. 65. Barium enema showing pressure on, and invasion of colon by malignant ovarian cyst.



FIG. 66. Utero-salpingography : 21-hour study showing peritoneal smearing ; the left ovary is completely outlined.

manner, and consider that it is as valuable to them as pyelography is to the genito-urinary surgeon and ventriculography to the neuro-surgeon. Other gynæcologists, however, seldom use the method except in the investigation of sterility. It is difficult to understand this divergence of opinion. One may presume that the patients of the first group are frequently subjected to this investigation when it is superfluous and therefore possibly undesirable. The second group of surgeons fail to avail themselves of a method of increasing diagnostic precision. The writer, being a radiologist, somewhat naturally feels that, providing an investigation *per se* is not detrimental to the patient, it should be used so that the pre-operative diagnosis is as accurate as possible. In short, diagnosis should be made whenever feasible before laparotomy and not merely at laparotomy.

The apparent prejudice of this second group of gynæcologists is probably due to their impression that uterosalpingography is somewhat dangerous procedure. Providing that due care and skill is given in the selection of patients for uterosalpingography then it may be said that the investigation is virtually without danger. The complications following uterosalpingography have been markedly exaggerated.

### The Indications for Uterosalpingography

Robins and Shapira (4) have given the indications for uterosalpingography very clearly and they state :—

“With proper respect for the risks and contra-indications hysterosalpingography may be very safely employed in gynæcology where it has a place in diagnosis, in prognosis, and, to a limited extent, in therapeutics. In general, its greatest usefulness is in sterility. Next in importance is its value in the menorrhagias and metrorrhagias. Thirdly, we may consider its advantages in the group of intrinsic or extrinsic tumours. Fourthly, we may emphasise its place in therapeutics by restoring permeability in some cases of tubal obstruction, and maintaining permeability after plastic tubal operation. Finally, we have found it of value in the tracing of sinus tracts which may have some connection with the genital tract.”

One might add two further indications: firstly, in the confirmation of suspected extra-uterine gestation (Greenhill (6)) and secondly, salpingography should be performed as a routine measure six months after operation for ectopic gestation.

### The Contra-indications for Uterosalphingography

The presence of acute or subacute infection of the vulva, vagina, uterus, tubes and general pelvic tissues is a definite contra-indication. Some authors do not advocate this investigation in the presence of pathological uterine hæmorrhage but this view is not held by all: Robins (4) holds that the rôle of uterosalpingography in the precise diagnosis as to the cause of hæmorrhagic lesions is important, and only withholds the investigation in severe hæmorrhage.

The injection should not be performed during menstruation, nor after curettage before full regeneration of the uterine mucosa has occurred, nor during pregnancy. Finally, the method is wisely not used in severe systemic diseases.

**The Dangers of Uterosalphingography.** There have been several reports of accidents and even occasional deaths after uterosalpingography. Such accidents are the spread of infection, tubal rupture, venous intravasation and oil embolism, abortions and septicæmia.

Gauss (7) collected and reviewed 3,000 cases in which uterosalpingography had been performed. In this series, there was a mortality of 0.11 per cent. and infection in 0.43 per cent. Many of the reported accidents are due to unskilful case selection, and most have followed the use of contrast media other than lipiodol.

Under modern technical conditions, with reasonable care in the selection of cases and in the actual injection technique, uterosalpingography may be regarded as a really safe procedure. The possible but improbable dangers have been grossly exaggerated. *Venous intravasation* has been reported but rarely with untoward sequelæ, such as oil embolism. It will occur more readily during menstruation and after curettage before mucosal regeneration. *Tubal rupture* has occurred when using too high a pressure with diseased Fallopian tubes and in tubal gestation. *Infection spread* is the commonest mishap, but it should never occur in a previously uninfected case. With an acute or subacute salpingitis the infective material may obviously be carried into the peritoneal cavity. *Abortions* have been reported, but Heuser (8) in the deliberate investigation of the uterine cavity in early pregnancy considered that abortion was rare.

**The Fate of Lipiodol.** There have been many reports on the finding of the iodised oil in the pelvic peritoneal cavity at laparotomy without any signs of peritoneal inflammation or irritation. Lipiodol is ejected from the tubes and uterus by their contractile

in normal and in most pathological conditions. When lipiodol is "spilled" into the peritoneal cavity there is a gradual lymphatic absorption and consequent removal and disappearance of the lipiodol. The oil may remain for long periods when encysted in pre-existing adhesion pockets or in dilated and blocked tubes.

### The Technique of Uterosalingography

This is a relatively simple procedure in expert hands. There are numerous excellent accounts of the technique in the literature to which the reader is referred. The technical failures are most often due to an inadequate occlusion of the external os uteri: a specially designed olivary cannula to prevent the outflow of lipiodol is essential. From the radiologists' viewpoint the instruments encroaching on the field should be of non-opaque material.

Whilst it is not essential, *the fluoroscopic control of the injection is highly desirable*; by this control, the radiologist is able to guide the gynæcologist throughout; in the early stages, artificial malposition of the uterus may be corrected; the most appropriate times for the taking of radiographs may be chosen and when the peritoneal spill has occurred the injection may cease, thus preventing the injection of a superfluous amount of oil. Information of some interest concerning the contractions of the uterus will also be forthcoming from this screen-controlled observation.

The injection should be made slowly, and films may be taken after fractions of the total to be used have been instilled: this fractional injection has certain advantages over total injection (Hyams (9)): the digital pressure on the syringe should be maintained throughout. If the body of the uterus is filled too rapidly, small polypi or submucous fibroids may be masked by the dense lipiodol.

When the injection has been completed, stereoscopic films should be taken before the pressure is released and in certain cases oblique and lateral views may be helpful. The instruments are then removed and the vagina cleared of any lipiodol. A further film may be taken one hour after injection. At twenty-four or forty-eight hours, after the vagina has been cleansed, final films should be taken whether there was, or was not, apparent tubal patency. The essential two radiographs are those taken at the completion of the injection and at the twenty-four or forty-eight hour period.

### Normal Appearances

The cervical canal has smooth margins and averages 4.0 cm. in length and is usually not more than 0.5 cm. wide. The normal uterine cavity has a triangular shape with the base at the fundus: the two sides are straight or somewhat convex outwards: the margins may show variable smooth contractions. The average normal dimensions are 3.8 cm. for the base and 3.4 cm. for the other two sides from the cornua to the internal os. The tubes are 7-10 cm. in length and are seen in their intramural and isthmic portions as fine opaque lines, which widen out considerably at the ampullary ends. Their course is very variable and even contortionate loops seldom have pathological significance. The cornual sphincters may sometimes be demonstrable just beyond the cornual angles as zones of constriction 1-2 mm. in length. In the tubes, peristalsis gives an impression of fine beading in the thin lumen.

The total capacity of the cervix, body and tubes in normal cases averages 6 c.cs. The uterine cavity is frequently enlarged in the presence of fibroids. The effects of drugs on the uterus and tubes may be accurately studied by uterosalpingography and serial radiography.

### Pathological Appearances

**The Cervix Uteri.** Pathological conditions of the cervix may be studied if Robins and Shapira's technique (4) is followed; these workers use a special adjustable cannula and non-opaque instruments when they wish to study the cervical canal as well as the body of the uterus.

**Carcinoma of the cervix** produces persistent and constant irregular marginal filling defects, similar to the appearances caused by carcinoma of the pylorus or colon in barium meal and enema investigations. Cervical polyps will give a smooth filling defect in the canal lumen.

**Endocervicitis** is usually accompanied by an increase in the width of the canal, up to 2.5 cm., and some increase in length. A characteristic feature is the appearance of striational markings at right angles to the long axis of the canal; this is due to an entry of the lipiodol into the cervical glands.

**The Uterine Body.** *Uterine malformations*, such as the infantile uterus, unicornuate uterus and uterus didelphys will be readily recognised. *Malposition* of congenital or acquired origin is

demonstrable especially with the use of stereoscopic A.P. and lateral views. It is important to be certain that instrumentation does not produce artificial malposition; this can be corrected by screen control. Further, a pathological malposition may be overlooked because of instrumental leverage.

Endometrial hyperplasia is recognised by the irregular, roughened and crenated margins of the cavity; a cornual block is usually present. *Uterine tumours* will produce varying appearances on uterography depending whether they distort the cavity or encroach upon it. Smaller fibroids may produce no abnormal appearances, especially in a subserous position. When tumours encroach upon the lumen they give rise to filling defects and the cavity is often enlarged with a capacity up to 40 c.c. or more. Small submucous fibroids produce a localised filling defect, which may be overlooked if the fractional injection is not used. Large fibroids which do not encroach upon the lumen cause a mass displacement, elongation and distortion of the cavity. The effects of parenchymal renal tumours on the pelvis and calyces as seen at pyelography are very similar to those produced by uterine tumours on uterosalpingography. *Retained conception products and moles* give rise to extensive multiple half-shadow defects in an enlarged cavity.

**The Fallopian Tubes.** *Tubal occlusion* can only be assessed with the adoption of perfect technique. Even without organic tubal pathological changes, the tubes may fail to fill because of (a) spasm, and (b) uterine atony. When spasm is thought to be present, the injection may be repeated after a course of anti-spasmodic medication, e.g., benzyl benzoate, given daily over a ten-day period immediately after menstruation.

Tubal occlusion may occur (i) at the cornual angle, leading to non-filling of the tube; (ii) at the isthmus, giving an abrupt cessation of filling; (iii) at the fimbrial end, with no peritoneal spill and varying ampullary dilatation; it is often difficult in this type of case to decide whether a peritoneal spill has occurred; the delayed radiograph is essential and with bilateral ampullary or fimbrial blockage, no peritoneal smearing will be seen.

Tubal occlusion is about four times as common at the fimbrial end and in the ampulla as in the isthmus and intramural portions.

Utero-tubal spasm is not rare and is often associated with dysmenorrhœa and may cause sterility. The spasm may occur at both cornua, at the internal os or involve the whole body of the uterus. With bilateral cornual spasm, neither tube will fill;

with ostial and general body spasm it is difficult (and may be impossible) to fill the body cavity.

**Hydrosalpinx.** Marked tubal dilatation will be seen, especially at the ampulla; the lipiodol will form multiple globules in the fluid, giving rise to a mulberry appearance. At a considerably later time, the droplets coalesce to form an opaque oval homogeneous opacity.

**Tuberculous salpingitis and pyosalpinx** characteristically shows tubal obstruction at varying sites associated with calcific *débris* opacities. *Tubal pregnancy* will show an atonic large uterine cavity with unilateral tubal obstruction; the obstructive defect is, in typical cases, trumpet-shaped. It is probably unwise deliberately to perform salpingography in suspected cases because of the friability of the tubal walls and consequent liability to rupture.

#### Extra-uterine and extra-tubal Masses

In these cases, utero-salpingography, with or without pneumoperitoneum in addition, may add useful information to that gained by clinical bimanual examination. Pressure displacement of the uterus and tubes, especially with ovarian and intra-ligamentous cysts, will show in many cases the details of the pathological anatomy. Unilateral elongation of one side of the uterus and an upward stretching of one tube will be seen typically in an intra-ligamentous cyst.

#### Uterosalingography and the Investigation of Sterility

Uterosalingography may be regarded as a most useful measure in the determination of the cause, and the site of the lesion responsible, in many cases of sterility. It is also a therapeutic measure in that pregnancy has frequently followed salpingography after long periods of sterility. The therapeutic action is probably solely mechanical, by clearing the tubes of thick inspissated secretions, by straightening up kinks from fine adhesions and by the breakdown of delicate stenosing membranes. Many authorities prefer to apply Rubin's test before proceeding to salpingography as the former investigation is devoid of any risk.

**Diagnostic Value.** Causes of sterility in the cervix, body and tubes may be clearly demonstrated, and the gynæcologist will be guided in his prognosis and in his choice of appropriate treatment. After plastic tubal operations for the relief of sterility, the transit of lipiodol may maintain patency. One must stress once again



the diagnostic pitfall of spasm simulating organic stricture and repeat tests after antispasmodic therapy, may be essential.

**Therapeutic Value.** Robins and Shapira (4) have performed utero-salpingography on 889 cases of primary or relative sterility. One hundred and thirty-four patients have subsequently become pregnant; of the 889, 497 had either bilateral tubal occlusion or such lesions that would only have permitted conception after surgical intervention. Of the remaining 392 cases with one or both tubes patent, or rendered patent by the lipiodol, no less than 34 per cent. have become pregnant.

The author wishes to acknowledge the help he has received in preparation of this chapter from the excellent article on "Uterotubography," by Robins and Shapira in "Diagnostic Röntgenology" (Editor, Ross Golden).

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## CHAPTER XV

### X-RAY THERAPY IN GYNÆCOLOGY

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#### Introduction

GYNÆCOLOGY appears to be one of the most fertile fields for development in radiation therapy. Advances in technique have occurred so rapidly in the last few years, and are likely to continue to do so, that dogmatic statements and teaching are seldom wise in radiation therapy; opinions change rapidly, and there is often a wide divergence of opinion held by respected authorities. The development of radiation therapy has considerably modified the scope of the indications for surgery which were generally accepted a few years ago.

As Martin (1) points out, good results in radiation therapy can only be realised with uniform success when a knowledge of clinical gynæcology is combined with an understanding of the mechanical, physical and biological problems inherent in the use of X-rays and radium. Co-operation between gynæcologists and radiotherapists must become closer than is frequently the case, and there is a need for medical men with special training both as gynæcologists and radiation therapists.

Although this chapter is devoted primarily to the use of X-rays, it would be both indiscreet and impossible to dissociate this use of X-rays from the use of radium. It is perhaps insufficiently appreciated that there is little essential difference between the biological action of gamma radiation from radium and of X-rays of a quality usually employed in X-ray therapy in gynæcology (X-rays produced by voltages from 150,000 to 800,000).

During the last few years the world-wide acceptance of the unit of X-ray dosage—the rontgen unit—has made the comparison of technical methods and results from different clinics far more easy. Recently, also, radium dosage can be judged in terms of the rontgen unit. The biological effect of the same number of rontgen (X-ray) units is not the same as of a similar number of rontgen (radium) units.

However, there is as yet no internationally accepted biological unit of dosage. The attainment of a standard biological unit would be highly desirable because the rontgen unit, a purely physical measure, produces different biological effects under different physical conditions. For example, a recognised "unit skin dose" may be produced by an exposure of 500 rontgens at relatively low kilovoltages producing relatively long wave-length X-rays, but at higher kilovoltages perhaps 1,000 rontgens may be necessary to produce the same biological skin effect, appropriate filtration being employed in each example.

It is a common practice to speak of an exposure or dose of, say, 700 rontgens. This expression conveys little scientific meaning unless it is specified whether this exposure is measured in air (without the backscatter of secondary radiation) or measured at the skin surface (including the backscatter). There is a considerable difference between an exposure of "r" measured in air and "r" measured at the surface, usually of the order of 80 per cent. Thus 500 "r" measured in air becomes approximately 800 "r" at the surface under technical conditions commonly used.

In gynæcological radiotherapy one is usually interested in *tissue-exposure* and dosage at a depth, and hence it is desirable to explain briefly the meaning of depth-dosage. By this term depth-dosage is meant the dose at a specified depth below the body surface. It is usually convenient to express this as a *percentage depth dose* indicating the amount of radiation delivered at and received by the tissues at a specified depth in percentage terms of that delivered at the centre of the skin field. The percentage depth dose under given technical conditions may be increased by:—

- (i) increasing the size of the field exposed;
- (ii) increasing the distance from the tube-focus to the skin surface;
- (iii) decreasing the wave-length of the X-rays, *i.e.*, increasing the impressed voltage producing the X-rays;
- (iv) increasing the filtration.

It is a cardinal rule of radiation therapy that all attempts to achieve optimum dosage at the site of the lesion should be made whilst doing a minimum of damage to overlying normal healthy structures. Hence in order to achieve, for example, a dose or tissue-exposure equivalent to 100 per cent. of the unit skin dose at a central pelvic tumour, multiple ports of entry through

different skin fields will have to be employed. If the percentage depth dose under given technical conditions is, say, 33 per cent., then three ports of entry will be required to give 100 per cent. of the unit skin dose at the central tumour. To achieve the same result with a smaller percentage depth dose, more fields will have to be exposed in a converging manner; fewer fields may be necessary with a higher percentage depth dose.

The quality of radiation used is dependent upon the voltage impressed to produce the X-rays and upon the intervening filters that may be employed. This quality is expressed quantitatively either in terms of wave-length, expressed in Ångstrom units, or in terms of the *half value layer* (H.V.L.). The H.V.L. is the thickness of material which reduces to half the intensity of a particular X-ray beam, and is often expressed in terms of millimetres of copper.

The exposure or dosage-rate is the exposure per unit time and is expressed in rontgens per minute. This is directly measurable with appropriate apparatus.

Finally, in this introductory explanation of the terms used in radiation therapy, we have to consider in what relation to time-factors X-ray exposures may be given. If the quantity of radiation required to produce an erythema of the skin (E.D.) in one dose (U.S.D.) is given in fourteen equal fractions daily over a fortnight, then no erythema will result; approximately twice the total amount will have to be delivered in equal daily doses to produce an identical erythema. Hence the spacing of dosage in relation to time is of the utmost importance.

The methods of dosage delivery used for gynaecological malignant conditions are briefly set out:—

(i) **Massive Single Dose Method.** The whole dose is planned to be given in one or two days. This is known as the Erlangen technique.

(ii) **Intensive Split-dose Method.** Daily exposures are given to the ports of entry over seven to fourteen days; all the fields may be treated each day, or the fields may be alternated.

(iii) **Protracted Fractional Method (Coutard).** As originally laid down, this method gave large doses (total) spread over a long period in small daily doses; the treatment period was often from twenty-one to forty days. The actual rate of dosage was very low (3 rontgens per minute), but this is not often followed. The Coutard method is widely modified, sometimes almost beyond recognition, to suit different requirements.

5.5 cm. from the mid-line only 2.25 to 2.5 skin erythemas dose were received.

The next problem will be the consideration of what might be regarded, generally speaking, as the "cancericidal dose." As a guide, the following opinions are quoted: Tod and Meredith (4), 6,000 r.; Berven (5), 4,500 r.; Baclesse (6), 4,500 to 5,500 r.; Martin and Quimby (7), ten skin erythema doses (approximately equalling 6,000 r.).

It becomes apparent that by radium treatment alone as it is now practised it is quite impossible to deliver to the peripheral parametrial zones and the lateral pelvic walls an adequate dose without severely damaging normal structures, *e.g.*, the bladder and rectum.

Further, glandular metastatic involvement will usually be ineffectively dealt with by intracavitary radium alone. To what extent is possible glandular involvement significant? Baisch (8) stated that in *operable* cases glandular metastases were present in 33 per cent., and in 5-18 per cent. when the parametria were microscopically free from disease. Lane Claypon (9) collected 1,215 operated cases from the literature and found that 33 per cent. showed gland involvement. An instructive analysis is given by Taylor (10) of the figures published by Kundrat (11), Pankow (12) and others after careful serial section examination which showed that:—

- (i) When both parametria were free of growth—16 per cent. showed gland involvement.
- (ii) When one parametrium was invaded—35 per cent. showed gland involvement.
- (iii) When both parametria were invaded—52 per cent. showed gland involvement.

Taussig (13) concluded that glands were involved in 25-33 per cent. of operable cases, in 45-50 per cent. of advanced cases, and in 66 per cent. of cases coming to autopsy.

Many of these glands will lie outside the zone of effective radiation from intracavitary radium, and it is again clear that radium application alone, even under ideal conditions, cannot possibly eradicate the lymph node metastases even within the true pelvis.

It might be argued that in Stage I cases with the growth apparently localised to the cervix, radium alone would be adequate. But this classification in stages is made solely on clinical grounds, and it is impossible to detect early gland involvement by clinical

methods. From the figures quoted we have seen that even with both parametria microscopically free of growth, 16 per cent. of cases show glandular metastases. It is therefore reasonable to suggest that even in Stage I cases transpelvic irradiation, supplementing intracavitary radium application, will be necessary to irradiate adequately the glandular metastases. This applies even more to Stages II and III of the disease.

There is, therefore, a clear theoretical case for using transpelvic irradiation supplementary to intracavitary radium, but it must be realised that this external irradiation will necessitate the exposure of a large volume of normal tissue to X-rays. The main problem is therefore one of applying adequate and effective radiation to the whole potential tumour-bearing area without damaging normal structures irreparably. Further, to quote Walker (17), "the importance of uniformity of dosage throughout the probable tumour area should be appreciated; if one part of the tumour receives a dose less than the lethal dosage, then the tumour will recur."

Many ingenious techniques have been devised at different centres in order to satisfy these criteria; some of these techniques will be mentioned later. The theoretical ideal at the present state of our knowledge is to regard intracavity radium and transpelvic X-radiation as complementary to each other with the radium application playing the dominant rôle. The radium treatment should be designed to eradicate the malignant cells at the cervix and in the immediate para-cervical zones; the X-ray treatment should be designed to bring the tissue dose to an estimated cancericidal level where this is not achieved by the radium, *i.e.*, in the lateral pelvic walls, peripheral areas of the parametria and in the various lymph node sites.

### Assessment of the Practical Value of Supplementary X-radiation

Almost all writers are convinced of the value of supplementary X-radiation. To quote but two reports, Lacassagne (2) reports from the Paris Radium Institute that since transpelvic irradiation has been used the five-year results have improved considerably. These results are given in table form in Chapter VII (p. 162). Morton (14) made a study of the five-year survivals among 79 patients treated with radium alone before 1931 and among 58 patients treated by radium and X-rays between 1931 and 1934. There was no appreciable change in the technique of the radium application in the two series. Of those treated with radium only,

15.2 per cent. were alive after five years and of those treatment by both methods 39.7 per cent. were living after the same period.

Some authors, including Heyman (15), are rather guarded in expressing unqualified approval of supplementary X-radiation. In a recent paper Tod (16), of Manchester, finds that judging on three-year results, cases in Stages I and II showed a 66 per cent. survival rate when treated with radium only, whilst a similar group treated by the combination showed a survival rate of 51 per cent. only. The use of X-rays in these stages actually appeared to decrease the survival rate; it is only fair to point out that the dosage aimed at is appreciably higher than in most clinics. For Stage III cases, however, the combination showed great promise.

The temporary disability and discomfort is much greater with adequate X-radiation than with radium alone, and the duration of bed-occupation is greatly lengthened. In some clinics an in-patient admission period of thirty to fifty days is found desirable.

**Technical Methods.** The X-radiation is usually applied by either the intensive split-dose method or by protracted-fractional methods or by modifications of these. There is considerable difference of opinion and practice as to whether the radium treatment should precede or follow the X-radiation. Those authors who advocate that the X-radiation should be given first point out that infection may be cleared up considerably and that the reduction in size of large vaginal masses permits of a better placement of the radium applicators, and that the actual mortality due to the radium application is decreased by preliminary X-radiation. Those who favour giving the radium first stress that as this is the more important of the two, the tissue tolerance should not be impaired by X-radiation which might necessitate incomplete radium treatment. Colloquially, X-ray therapy must not be allowed to "queer the pitch" for full radium application.

It is not possible to give more than one or two examples of technical methods as used by different workers.

(i) *Walker, Royal Infirmary, Edinburgh.* This technique is an example of a carefully considered method based on sound physical investigation. The object is to deliver a cancericidal dose throughout the tumour bearing area; this dose is considered to be 10,000 rontgens (radium) and 5,000 rontgens (X-rays) with X-rays of a quality H.V.L. 2.5 mm. copper given over one month.

The patient is examined and the radium applicator arrangement decided upon. The treatment is then planned thus :—

First half X-ray course spread over . . .	12 days.
First half radium application over . . .	2 days.
Second half X-ray course spread over . . .	12 days.
Second half radium application over . . .	2 days.

When proliferative vaginal masses are present which make radium application inefficient, then the whole X-ray course is given first, followed by half the radium dose, the second half being given six weeks later. The X-ray delivery is by three anterior and three posterior fields; the central fields (both A and P) measure 15 by 10 cm. with the longer dimension transversely across the pelvis, and these are divided by a central lead mask 4, 5 or 6 cm. in width to screen the central cervix area. Because of the central masking, the six fields virtually become eight, with the addition of the two anterior side-fields and two posterior side-fields, each 10 by 5 cm. in size. The maximum X-ray exposure is reached 7.0 cm. from the mid-line. All the fields are treated daily for five days in each week.

(ii) *Arneson and Quimby Technique* (18). Many radiation therapists base their technique on the isodose studies for various field arrangements worked out by Arneson and Quimby. The X-ray contribution to the total dosage received by the various pelvic viscera in a patient measuring 25 by 35 cm., using 200 kV. with a filtration of 0.5 mm. copper + 2 mm. aluminium, 70 cm. focus-skin distance, with the skin dose ("r" in air + backscatter) considered as 100 per cent., is as follows :—

Field arrangement.	Cervix	Para- metria	Bladder and rectum
A. Two fields, 1A and 1P, each 20 × 15 cm.	60-70%	10% †	70-90%
B. Four fields, 2A and 2P, each 10 × 15 cm.	60-70%	40% †	60-70%
C. Four fields, 1A and 1P, of 15 × 20 cm., with two lateral of 10 × 15 cm.	80%	80-95%	80-95%
D. Six fields, 2A and 2P, each 10 × 15 cm., with 2 cm. interval at mid-line, with two lateral of 15 × 10 cm.	70-80%	80-90%	60-80%

In arrangements A and B the dosage at the parametria is too low; in C it is adequate at the parametria but too high at the bladder and rectum; in D, the six-field method, it is high at the parametria and relatively low at the bladder and rectum. This



six-field arrangement is certainly the best under these conditions. It should be pointed out that the more central fields are directed vertically downwards and do not converge towards the cervix.

(iii) *Healy (19), New York Memorial Hospital.* The X-ray therapy is given first under the following conditions: 200 kV., 0.5 min. Cu + 2 mm. Al filtration, 70 cm. focus-skin distance, four fields (2A and 2P) each of  $15 \times 15$  cm. Each side of the body (two fields) is treated on alternate days with 200 r. per field until a total dose per field of 2,000–2,500 r. has been given in twenty to twenty-five days.

By this means approximately four to five erythema doses are given to the cervix and parametria and the periphery of the pelvis receives three erythema doses. Ten days later the intracavitary radium is applied, bringing the total dose at the cervix to fifteen erythema doses. This is an example of a technique in fairly general use.

(iv) *Schmitz and Sheehan (20), Mercy Hospital, Chicago.* For the last few years these authors have been supplementing radium application with X-rays produced at 800 kV. (the so-called super-voltage therapy). At 800 kV. maximum the quality of radiation employed has an H.V.L. of 8.2 mm. of copper and a wave-length of 0.0128 Angstrom units. The delivery rate is 36 rontgens per minute when measured in air and 44 rontgens per minute with backscatter. The percentage depth dose at 10 cm. depth is 54 per cent. for a field of 300–400 sq. cm. in size. The tolerance skin dose is 4,000 rontgens when given in ten fractions at forty-eight-hour intervals. Using two fields, the tissue dose centrally and laterally in the true pelvis is 4,000 r. under these conditions.

A brief note as to the five-year results attained by these authors on a small series are worthy of note and indicate the potentialities of this type of radiation. These results are given below in table form:—

Clinical stage.	I	II	III	IV.	Total
Number of cases . . .	2	1	9	14	26
Well five years . . .	2	1	7	2	12
					= 46.1%

The techniques quoted above have been chosen solely as fairly typical examples of modern radiotherapeutic practice. It is

perhaps important to stress that individualisation rather than standardisation in the technical application of combined radium and X-ray therapy is the object at which to aim. All techniques devised should be based on sound dosimetric chart work such as that produced by Arneson and Quimby (18). and Tod and Meredith (4).

In conclusion, it may be stated that there is wide agreement that carcinoma of the cervix should usually be treated by the combination of intracavitary radium application with transpelvic irradiation, either by X-rays or tele-radium. It is, however, admitted that the adequate complementary technique is difficult to deliver without a considerable undesirable reaction in the patient. It seems reasonable to state that whilst only 40 per cent. of cases are potentially curable by radium alone, perhaps 80 per cent. of cases are potentially curable by the combination of methods (Taylor (10)) when a general optimum technique has been realised.

## 2. X-ray Therapy in Combination with Surgery

Radical surgical operations are performed relatively infrequently in modern practice. Many surgeons skilled in the Wertheim operation have gone over to radium therapy, but in certain clinics the Wertheim or Schauta operations are still performed. There is a strong case for both pre-operative and post-operative irradiation of the whole pelvis in conjunction with radical surgery, but owing to the waning popularity of the Wertheim operation in those years in which X-ray technique has been improving there are few important statistical contributions relating to the curative value of surgery in combination with X-ray therapy.

On theoretical grounds there is a good case for routine post-operative irradiation, though some authorities consider that the risk of fistula formation is increased. By pre-operative irradiation operative technique is sometimes facilitated and the relative improvement in the degree of infection is worth achieving.

## 3. X-ray Therapy Alone

X-radiation used alone may be employed with either (i) a radical or curative intention or (ii) as a palliative measure in advanced cases.

(i) **Radical X-ray Therapy.** Owing to the superior results given by radium application and the increased availability of radium,

X-ray therapy as a sole measure has rightly fallen into relative disuse. But because a newer method is more successful an older method does not necessarily become disreputable. Incidentally, the proved though somewhat limited value of X-radiation alone lends weight and argument to its employment in combination with radium.

In 1931 Wintz (21), of Erlangen, published his results in 837 cases of carcinoma of the cervix, the great majority of which were treated by X-rays alone, a minority being treated with small supplementary radium doses in addition. Wintz published the following figures—

Carcinoma of cervix	161	Five-year cures of 837 cases seen = 19·2 per cent.
Carcinoma of body	16	Five-year cures of 209 cases seen = 22·0 per cent.

Wintz practised a "massive dose" technique in two stages, each being completed in from twenty-four to forty-eight hours; in the first stage the treatment was directed at the cervix and in the second at the parametria.

Baclesse (23) has reported that in a series of 63 advanced cases treated by X-rays alone, 9 cases, *i.e.*, 14 per cent., were free of disease after five years. The results of Gunsett (22) may also be mentioned; in cases with broad ligament involvement, 22·2 per cent. were alive and well after five years.

Although the superiority of the combination of radium with X-rays is unchallengeable, it will be interesting to observe the results of X-radiation alone at 800,000 to 1,000,000 volts when statistical case numbers are adequate. The wave-length of X-rays produced at 1,000 kV. is beginning to approach the shortness of the wave-length of the gamma rays of radium.

(ii) *Palliative X-ray Therapy in Advanced Cases.* Providing that radical dosage is not attempted, the condition of many advanced cases can be ameliorated appreciably by X-radiation. In a case regarded as hopeless it is obviously unwise to irradiate as heavily as in a potentially curable case; "radical" irradiation is undoubtedly an ordeal for the patient.

However, with moderate dosage, pain may be appreciably relieved, the discharge and hæmorrhage lessened and life which is tolerable may be prolonged. In selected cases urinary obstruction may be relieved.

Behney (24) found that in a series of advanced cases (1D of the

American classification) those receiving X-ray therapy lived 4.6 times as long as those having no treatment.

The reference of advanced cases to a radiotherapeutic department should be carefully weighed up; in a department working to full reasonable capacity the reference and consequent treatment of such advanced cases may impair the efficient attention that can be given to other cases of malignant disease. When symptomatic palliation only is sought the radiotherapist should be fully aware that this is the object; the days when radiotherapy departments were regarded as dumping grounds for hopeless cases is surely over.

## CARCINOMA OF THE BODY OF THE UTERUS

The treatment of carcinoma of the body of the uterus in modern practice is either

(a) Surgical, by panhysterectomy.

(b) Intracavitary radium application (see Chapter VIII).

X-radiation may play an advantageous rôle in combination with either of these dominant methods. With surgical treatment X-radiation may be given either pre-operatively or post-operatively (or both). With radium treatment supplementary X-rays in general follow the lines set out in the section on Carcinoma of the Cervix.

A few examples of methods used by certain authors may be quoted. Clark and Norris (25) advocate the use of preliminary X-radiation followed six weeks later by panhysterectomy. Healy (19) finds that with such a method half the uteri removed at operation show no remaining malignant changes. Morton (26) advocates panhysterectomy for cases in which the growth is confined to the uterus and for more advanced cases uses intracavitary radium and external X-radiation. Healy follows radium application by X-radiation as for cervical cancer, as shown on p. 322.

Voltz (27) reports a 62 per cent. absolute cure rate and believes that his results have been definitely improved by irradiating the pituitary body: this is done with a two-field technique (each field 6 by 4 cm. over the lateral temporal areas) delivering 150 rontgens (or 25 per cent. unit skin dose) at the pituitary.

An excellent paper by Heyman, Reuterwall and Benner (28) has recently appeared. Heyman advocates intracavitary radium application, combined with hysterectomy in cases of failure, as

the method of choice except in patients particularly well suited to surgery.

### UNCOMMON UTERINE TUMOURS

**Sarcoma of the uterus** is a radiosensitive tumour, but radical surgery may be regarded as the only successful single curative method. Intensive post-operative X-radiation should be given to the pelvis by a four- or six-field method, aiming at a tissue exposure of 1,800–2,000 rontgens throughout the pelvis.

**Endometriosis.** Endometrioma masses become smaller or cease to produce symptoms after the menopause. Hence in women over forty years a radiation-induced menopause may be advantageous. Further, X-ray therapy is especially useful as endometriomatous masses may grow in situations where surgical removal is impracticable.

**Chorio-epithelioma.** Ewing's classification will be used to indicate the appropriate therapy for the different forms. *Chorio-adenoma* though invasive is relatively benign. Hysterectomy gives good results; intra-uterine radium application is often impracticable because of profuse hæmorrhage. *Syncytioma* may be treated by thorough curettage followed by intra-uterine radium. *Chorio-carcinoma* is a highly malignant tumour. Most surgeons advocate hysterectomy, but Ewing cannot find any record of an operative cure. Radiation therapy has produced a small number of reported cures. The technique of choice would appear to be the combination of intra-uterine radium with external X-radiation on the lines of the treatment for uterine fundus carcinoma.

### OVARIAN CARCINOMA AND OTHER MALIGNANT TUMOURS

There appears to be general agreement that except in the most advanced cases, surgical extirpation should always be attempted in malignant ovarian diseases. Surgery has not, however, provided a high percentage of cures. Heyman (29) states that by adding radiation therapy to surgery the Radiumhemmet Staff obtained 65·6 per cent. of five-year cures in 32 cases. Wintz (30) by irradiating inoperable cases showed 40 per cent. to be alive after three years and 23 per cent. after five years; he gave 110–115 per cent. of the erythema-skin-dose to the pelvis in three days, repeating the course in six weeks and again in five weeks. Walter, Bachman and Harris (31) contrast surgery alone—63 cases of which 6·3 per cent.

years—to the results of surgery with post-operative radiotherapy (usually X-rays) 61 cases of which 29 per cent. were alive in five years when treated with “adequate X-rays,” and 10 per cent. were alive in five years with “inadequate X-rays.” These authors strongly advocate maximal X-ray dosage whenever possible and feel that palliative therapy has little use.

Many techniques have been described; three modern methods of application will be briefly mentioned. Harris and Payne (32) adopt a saturation technique at 165 kV., 1,600–2,000 rontgens being delivered to the centre of the pelvis in four weeks. Each of the four fields used is treated every second day with doses large enough to build up the required tissue dose. Healy's technique (19), as described in the section on carcinoma of the cervix, is excellent for ovarian tumours which are limited to the pelvis. Martin (33) uses 220 kV., 2.25 mm. Cu + 1 mm. Al filtration, 50 cm. distance and four fields each of  $15 \times 15$  cm. One area receives 200–300 rontgens each day until 1,800–2,000 rontgens have been delivered centrally in the pelvis.

The principles of the Coutard technique should apply well in the treatment of these cases.

## CARCINOMA OF VULVA AND VAGINA

**Carcinoma of the Vulva.** The primary lesion may be treated by surgical excision or by radium application from external plaques or interstitial needling. Whether dissection of the groin glands is used or not, these lymph node areas should be fully irradiated by X-rays.

**Carcinoma of the Vagina.** The results of treatment of vaginal carcinoma are generally very poor. Here, again, the chief use of X-rays lies in the control of the lymph nodes in both groins.

## THE ACTION OF X-RAYS ON THE OVARIES

The changes resulting from irradiation of the pelvis in nearly all benign gynaecological disorders may be ascribed to the action of X-rays on the ovaries. It has been known that the ovaries are highly radiosensitive since the work of Halberstaedter in 1904.

Large doses of X-rays will completely destroy the primordial follicles, whilst moderate doses inhibit their development. The small doses given during “mild irradiation”—the so-called

### Results of Mild Irradiation

Up to 1939 Kaplan (40) had treated 194 cases with an adequate follow-up control in 156 cases. In 103 cases menstruation was regularised; in this group no less than 50 women became pregnant, many after long periods of sterility. No improvement was found in 53 cases. None of the patients was in any way harmed by the procedure; only one fœtus was abnormal, and all the babies born were healthy. Martin (33) has noted that in many of his cases a return of menstruation coincided with a marked relief from periodical headaches. If only a temporary return of the menses occurs, the dosage may be repeated at a later date.

**Technique and Dosage.** Two examples will be given. Kaplan (41) always irradiates the ovaries and sometimes the pituitary also. With the following conditions, 200 kV., 4 milliamps., 0.5 Cu + 1 mm. Al filtration, 30–40 cm. focus-skin distance, four fields (two anterior, two posterior—each of  $9 \times 12$  or  $15 \times 12$  cm.), 75–150 rontgens (in air) are given at weekly intervals for three weeks, alternating the anterior and posterior fields each week. The pituitary is sometimes treated with similar doses from two lateral temporal fields.

Martin (33) aims at giving 5 per cent. of the erythema dose to the ovaries; with his conditions this implies giving 83 rontgens to the skin over a  $20 \times 20$  cm. field to deliver 30 rontgens to the ovaries. He also irradiates the pituitary, delivering 30 rontgens to the gland from two lateral skull fields. Bruck and Fruchter (42) have recently published an interesting report on the results of mild irradiation to the ovary and pituitary in 108 cases of various functional disturbances. There were 40 cases with deficient menstruation and sterility; in two-thirds regular normal menstruation was restored, and in half of these pregnancy followed. Thirty-four cases showed deficient menstruation without sterility; in half of these cases normal menses were restored. The other case groups showed hypermenstruation with sterility, regular menses with sterility and severe menopausal symptoms; in these groups just under half the cases were definitely benefited.

### TREATMENT OF UTERINE HÆMORRHAGE WITHOUT DEMONSTRABLE PATHOLOGY

The treatment of uterine hæmorrhage without demonstrable pathology, a condition which has received many different names, *e.g.*, metropathia hæmorrhagica, ovarian hæmorrhage, is a most useful field for radiation therapy. Shaw (43), in an excellent

paper, analysed 200 cases and found no demonstrable lesion in 35 cases and a true endometritis in 13 cases; the remaining 152 cases he divided into four groups—metropathia hæmorrhagica, epimenorrhœal type, hypomenorrhœal type and the metorrhagic type.

From a radiation therapeutic standpoint, the cases may be considered in two groups:—

(i) Those patients of over forty years of age in whom an artificial menopause may be induced.

(ii) Those patients of under forty years of age in whom menstrual activity should be preserved.

**Irradiation in Patients over Forty Years.** The problem in this group is relatively simple. X-ray therapy alone may be used, or a combination of intra-uterine radium with X-rays. Martin (33) uses the combined method: after dilatation and curettage, a 50 mgm. radium capsule is placed well up at the fundus and left for twenty-four hours. On the afternoon of the second day a skin dose of 540 rontgens is given through an anterior  $20 \times 20$  cm. field, at 200 kV., with 0.75 mm. Cu + 2 mm. Al filtration.

A further discussion as to dosage and technique is given in the section on the treatment of fibroids.

**Irradiation in Patients under Forty Years.** This is by no means a simple problem. A short statement of the methods used by various authors will be given. Clark and Norris (25) give 200–300 mgm. hours of intra-uterine radium; Neill (41) by the same method gives a dose averaging 580 mgm. hours. Bowing, Fricke and Desjardins (45) found that the hæmorrhage was controlled in 98 per cent. of 295 cases by small to moderate doses of intra-uterine radium. Floris and Businco (46) and Ford and Drips (47) have obtained good results by irradiating the pituitary, giving about 10 per cent. erythema dose at the sella.

There is considerable evidence that irradiation of any part of the body may produce a temporary arrest in the hæmorrhage. Martin (33) reports good results from the use of intra-uterine radium (300–500 mgm. hours) followed by pituitary X-radiation. In almost all cases control of the hæmorrhage lasts from six to twelve months, after which the menorrhagia may recur.

## THE TREATMENT OF FIBROIDS

All observers agree that fibroids become appreciably smaller after irradiation and after the menopause. The main effect of radiation is certainly on the ovaries; considerable X-ray doses



are required to produce any direct changes in the fibroids themselves. Clark and Norris (25) are firmly of the opinion that the considerable benefit given by radiation results from the ovarian effect. These authors and Lockyer (48) state that 20–30 per cent. of all fibroid cases are suitable for radiation therapy; Corscaden (49) puts the suitability figure at 50 per cent.

**Contra-indications for Radiation Therapy.** Clark and Norris (25) give the following contra-indications for radiation therapy: (i) Age less than forty years; (ii) a doubtful diagnosis; (iii) the presence of other abdominal conditions demanding surgery such as ovarian neoplasms; (iv) the presence of degeneration or calcification of the fibroids; (v) pedunculated subserous and submucous fibroids; (vi) rapidly growing and very large fibroids; (vii) the presence of pressure symptoms, especially pain and urinary disturbances; (viii) the presence of pelvic inflammatory conditions; (ix) radiophobia or marked neurological instability in the patient; and (x) pregnancy.

In short, the ideal case for radiation therapy is one in which the fibroid is of moderate size and in which bleeding is the only serious symptom.

The age factor is very important. Whereas the induction of a temporary artificial menopause produces a lessening of the bleeding and a decrease in size of the fibroids, it is too unreliable and the benefit is too transient to be of real value. In contrast, the permanent castration is almost always effective. Hence the problems in patients over forty and in those under forty are quite different.

### **Advantages of Irradiation over Surgery**

In properly selected cases radiation therapy has certain advantages over surgical treatment for the following reasons:—

(i) Radiation is often applicable where surgery is contra-indicated because of generalised diseases.

(ii) Surgical treatment carries an operative mortality of about 2 per cent. even in the best hands; the radium application mortality is well under 1 per cent. and the X-radiation mortality is nil.

(iii) Post-operative complications are fairly common; post-X-radiation complications are rare.

(iv) Surgery demands one month's hospital admission, radium application three to four days, whilst hospitalisation is not essential for X-ray therapy (though in some cases desirable).

(v) Radiation treatment will permanently control the bleeding; conservative myomectomy is often followed by further hæmorrhage and the growth of further fibroids.

### Statistics of Results

An evaluation of the results is not always easy because of the variation in what is accepted as a "cure." Many authors term a "clinical cure" to have resulted when the hæmorrhage is permanently controlled.

Ammon (50) collected nearly 8,000 cases of fibroids and the hæmorrhagic metropathies treated by radiation methods and found that 90·2 per cent. showed "clinical cure." The results of Nemenow (51), with his review of the results obtained by Strassmann, Kaufman, Kupferberg and Martindale give a further 2,328 cases, of which the average "clinical cure" percentage was 97·4 per cent.

The control of hæmorrhage is, of course, only a control of a cardinal symptom of fibroids. The disappearance of the tumour is not so easily accomplished. Nemenow (51) states that the tumour disappeared in 37·5 per cent. of his cases; many authors give higher percentages. Gambarrow (52) reports 800 cases in which amenorrhœa was achieved in 95·5 per cent., in 35 per cent. there was complete disappearance of the tumour, and in 55 per cent. there was considerable reduction in the volume of the mass.

Polak (53) followed 206 cases treated by radiation and the results were excellent in all but 6 cases; each of these had submucous fibroids.

Summing up, it may be said that X-rays or radium properly applied will cause the hæmorrhage to stop in 95 per cent. of cases and an appreciable reduction in the size of the tumour in 80 per cent.

### Technique of Radiation Therapy

Only techniques suitable in women over forty years of age will be considered. X-rays or radium will be found to be equally efficient. In favour of using radium is that the hæmorrhage ceases immediately, whereas bleeding may continue in a lesser degree for a few weeks after X-ray therapy, and that the preliminary curettage will ensure that a fundus carcinoma is not being overlooked. In favour of X-ray therapy is that little or no hospital admission is necessary.

Whilst some of the earlier techniques at moderate voltages have

been productive of good results (Béclère (54)), only techniques under modern condition of "deep" therapy will be mentioned. Based on the figures of Seitz and Wintz (34) and on Schneider's (35) calculations, which, though not necessarily accurate form a useful guide, it may be said that 22.0 per cent. of the unit-skin-dose (as defined by Martin) will be required in a woman of fifty-six to sixty years with a fibroid reaching to the upper level of the symphysis; in contrast, the ovarian dose required in a young woman aged twenty to twenty-five years with a fibroid reaching to the umbilicus will be 46 per cent. U.S.D.

Many authors have pointed out that the sterilisation dose of Seitz and Wintz is adequate for pathological ovaries, but is inadequate for normal healthy ovaries. This is emphasised by Gauss (55) and Pickhan (56) in a review of the results from ninety German clinics with adequate facilities.

Martin (33) employs intra-uterine radium plus external X-radiation, but where the latter alone is used he gives 830 rontgens to the ovaries through two large (20 × 20 cm.) fields, one anterior and one posterior; in a patient of average size this implies giving a skin dose of 480 rontgens to each field. Peck, Greer, Kretschmar and Brown (57) employ distinctly higher doses which are indicated, with the results, below. In treating a heterogenous group of 334 cases of benign pelvic lesions they used these conditions: 200 kV., 50 cm. focus skin distance, 0.5 mm. Cu + 2 mm. Al filtration, 30-50 r. per minute delivery, 300-400 sq. cm. ports, both anterior and posterior. In a group of 72 cases in which the ovarian exposure was 625-749 rontgens all the cases were castrated; 34 of 36 cases were sterilised with doses of 500-624 rontgens, and 90 per cent. of the cases were sterilised with doses of 375-499 rontgens. Thus Peck and his co-workers found that ovarian castration was not successful in 10 per cent. of cases even with ovarian exposures appreciably higher than the calculations set down by Seitz and Wintz.

### CHRONIC PELVIC INFLAMMATORY LESIONS

The problems of radiation treatment of malignant disease have commanded so much attention that radiation therapy of chronic inflammatory lesions has suffered comparative neglect. This neglect is unfortunate for there is little doubt that in certain chronic inflammatory disorders X-ray therapy produces most useful results.

Chronic pelvic inflammatory lesions, whether of gonococcal, pyococcal or tuberculous origin, or consequent upon the complications of abortion and child-bearing, give rise to severe ill-health in affected women. Pain, backache, menorrhagia and numerous pseudo-neurotic complaints result in marked incapacity in many patients.

The ordinary forms of gynaecological treatment, whether conservative or surgical, are often most disappointing in their results. Radiation therapy may be of definite value in some of these cases, but the chronic gonococcal forms do not usually respond well.

Irradiation may be used in one of three ways : (i) mild irradiation ; (ii) induction of temporary menopause ; (iii) unilateral ovarian castration.

Some of the published results using these three different methods are given below, and whilst they should be accepted with some reserve, these results at least justify a wider use of X-ray therapy for chronic pelvic inflammatory lesions, especially in cases which prove resistant to other forms of treatment.

**Mild Irradiation.** Holzknacht (58) has reported the following results from his considerable experience : about one-third of the cases are in no way benefited by mild irradiation ; in one-third of the cases there is a rapid good result, the symptoms disappearing completely, as it were by " crisis " : in the remaining one-third the duration of the illness is lessened considerably to a fraction of its usual course. Many other therapists have reported similarly encouraging results except with the gonococcal cases. Schmitz (59) recommends that in tuberculous cases 5 per cent. of the erythema dose be given to the ovaries at three-weekly intervals.

**Temporary Sterilisation.** Pelvic inflammatory lesions undoubtedly undergo exacerbation during menstruation ; theoretically, therefore, a cessation of menstruation should lead to symptomatic relief. Guttman and Bott (60) give a careful survey of their results by temporary sterilisation. The non-gonococcal and tuberculous cases showed marked symptomatic relief during the period of amenorrhœa, and this relief usually persisted after the return of menstruation. In the gonococcal cases, whilst there was relief during the amenorrhœa, the symptoms returned with equal severity with the return of the menses.

Menstrual psychotics showed marked benefit which persisted. In this paper of Guttman and Bott, much interesting information is given concerning the symptoms referable to the temporary

menopause and to the nature of the menses when re-established after the temporary cessation.

A satisfactory ovarian exposure is 150 rontgens to produce four and a half to six months' amenorrhœa. By using two large fields, one anterior and one posterior, each of  $20 \times 20$  cm., at 200 kV., with 0.75 mm. Cu + 1.0 mm. Al filtration, at 50 cm. distance, with a skin dose to each field of 210 rontgens, this ovarian dose is achieved.

**Unilateral Castration.** Some authors advocate a total castration dose to one ovary; because all the follicles in this ovary are destroyed there is no danger to possible offspring. Great technical care is required to ensure that the other ovary is not damaged. Obviously, though limited, the menses will not cease if the other ovary is normal. Marum (61) delivers 30 per cent. E.D. to one ovary and reports a decrease or absence of menstrual pain with partial or complete regression of the chronic inflammation. Seisser (62) has obtained a complete symptomatic relief in 89 per cent. of 110 cases treated by unilateral castration. This form of therapy is especially indicated when the inflammatory lesion is mainly unilateral.

### **Pruritus of the Vulva and Anus**

This distressing condition often responds well to fractional X-ray dosage. In some cases a complete cure results; in the majority a marked temporary relief of the symptoms is followed by a recurrence; in about one-third of the cases there is no beneficial response. In the latter group it is useless to persist with X-ray therapy. In the cases showing temporary benefit a recurrence will usually show a gratifying response.

A suggested scheme of treatment is given below: three doses of 200–230 rontgens are given at weekly intervals for three weeks, using 0.5 mm. Al filtration at 90–110 kV., followed if necessary by a larger dose, using higher filtration (400 rontgens with 3.0 mm. Al).

Such a course may be repeated after three to four months if there is a tendency to recurrence. Resinol ointment has been found to be most helpful during the course of X-ray therapy.

The low-voltage contact therapy method is particularly suitable in pruritus cases.

The writer wishes to acknowledge the considerable help he has received from Dr. Charles L. Martin's chapter in "Clinical Roentgen Therapy" in the preparation of this chapter.

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## CHAPTER XVI

### PHYSIOTHERAPY IN GYNÆCOLOGY

By Dr. JUSTINA WILSON, F.R.C.P. (Edin.), D.M.R.E. (Cambridge)

Conservative treatment in gynæcology has not made as much headway in England as it has abroad during the last two decades.

This is partly due to the advances made in surgical technique and asepsis, partly to insular conservatism; largely also to the unpopularity of physiotherapy in England.

There are comparatively few gynæcological surgeons in England who would agree with those distinguished teachers, Peham and Amreich, that 80 per cent. of tumours of the adnexa can be cured by conservative treatment only.

There are many groups of cases where surgical operation must always be the method of choice and the only treatment that will cure, but there is a large field of minor gynæcological troubles where conservative methods would be more used if it were realised that modern methods of physiotherapy do not necessarily make larger demands on time and hospital beds than do surgical ones.

Physiotherapy, unfortunately, is a plant of tardy growth in England. With the exception of a handful of specially qualified men and women; the medical profession, is singularly indifferent to and ignorant of its possibilities and methods.

This is regrettable, for during the last ten years abroad it is just in the treatment of gynæcological diseases that physiotherapy has made its most notable advances and has practically revolutionised the treatment of acute inflammatory conditions.

Pelvic hyperæmia is as old as Hippocrates and is an important principle in the treatment of inflammation.

Long hot douching was one of the earliest attempts to apply heat to the interior of the pelvis. Done with judgment and care and without too much pressure it relieves pain and inflammation. Douching, however, may be a two-edged sword. The two commonest types of pelvic congestion are gonococcal salpingitis and post-partum cellulitis. In both of these douching may do harm by washing infection upwards into the uterine cavity and even beyond.

Other methods which have all been tried with some success



for inducing hyperæmia are local hot air baths, infra-red and visible light, and fangopacks.

The Elliott bag represents an advance on douching. Here hot water is enclosed in a specially constructed distensible rubber bag with inlet and outlet tubes for circulating hot water. Inserted into the vagina it can be further distended. Its two advantages are the possibility of applying a high degree of heat for a long time and the pressure it exerts, which distends the upper part of vagina and fornices. The initial temperature of 115° F. to 120° F. is controlled by thermostat and can be maintained for an hour. It produces hyperæmia in vagina, uterus and rectum but has less effect in the pelvic peritoneal cavity. It also brings about an increase in the leucocyte count and a profuse cervical discharge is the immediate result.

Technique is of importance. The treatment must be given slowly, and patients should be watched for signs of reaction as some are intolerant to distension; and sloughing and ulceration are not unknown.

It is used in the treatment of inflammatory lesions generally, but discernment must be exercised in the selection of suitable cases. We have to distinguish here between post-abortive and gonococcal types of infection. In the former streptococcal infection is common, the organisms penetrating the uterine wall and producing induration of the pelvic connective tissues which become adherent to the uterine and pelvic walls so that dense masses of adhesions may be formed. Such cases are not suitable for Elliott treatment, which acts best in gonococcal infection which affects the tube primarily and ovary and peritoneum secondarily, producing softer tubo-ovarian masses higher up in the pelvis which do not adhere to uterine and pelvic walls.

On the whole the Elliott bag is an ingenious method of applying heat to a limited area. But it does not cause a deep and homogeneous heating delivered not only to the focus of inflammation but to a wider area of the surrounding pelvic tissues. There it fails.

### DIATHERMY

When diathermy was introduced and it became possible to use high frequency currents of medium frequency of about one million oscillations per second with wavelengths of 600 to 300 metres, high hopes were entertained as to its deep and far-reaching action in inducing pelvic hyperæmia.

But as regards homogeneous depth effect diathermy has been

a great disappointment. It has good results and is still used in the treatment of infections, chiefly gonococcal, and in the application of heat to the urethral and cervical canals by the method introduced by the late Dr. Elkin Cumberbatch and Dr. C. A. Robinson.

Diathermy currents, however, are not able effectively to heat deep-seated organs or parametric tissue.

There is no getting over this failure of diathermy to heat deep-seated organs and tissues, so that as regards depth effect it is not a great improvement on the Elliott bag treatment. And, though diathermy will relieve pain and cause improvement, the good it does is not permanent.

Some years ago the author treated a series of some 40 cases of primary and recent gonococcal infection by urethral and cervical diathermy. A thorough follow-up of these cases showed that tubal inflammation was by no means uncommon.

In the cases in which tubal complications did not occur, diathermy certainly caused temporary improvement. But recurrences occurred in all the discharged cases, some in a few months, others within a year. The best results were seen in the treatment of gonorrhoeal arthritis where urethral treatment only was given.

The problem of deep heating in a complicated organism like the body, which consists of imperfectly connected resistances and capacities that exist between adjacent conducting and semi-conducting layers, cannot be solved by a current that is limited by tissue resistance and by its predilection for paths of highest conductivity, always avoiding the resistance of bone, fat, capsules and membranes, which it fails to penetrate.

But when in 1926 at Jena, Esau and Schliephake succeeded in generating ultra-short high-frequency currents of 10 to 100 megalocycles endowed with sufficient energy to penetrate all structures in the condenser field, it was found that deep-seated organs, the adnexa and even parametric tissue, could be effectively and evenly heated.

### ULTRA-SHORT-WAVE THERAPY

In the ultra-short-wave high-frequency field, with its frequencies of 10 to 100 million oscillations a second, the physical laws of Joule and Kirchoff no longer hold. Here the current divides into two components, the current of conduction and the current of capacity or displacement, so that the difficulty of passing through insulating layers of glass and rubber, or resistant masses of bone,

### Ultra-Short-Wave Therapy in Gynæcological Practice

Here the chief indications are inflammatory tumours of the adnexa and pelvic cellulitis. The immediate result of the analgesic and antispasmodic qualities of the ultra-short-wave current is freedom from pain. This occurs very soon. There is rapid improvement in all subjective symptoms and a definite fall in temperature after two or three treatments.

Eight years ago the author visited Schliephake's clinic at Giessen and was greatly impressed by the results seen. There were only a few gynæcological cases being treated at that time but the author received further insight into these new methods in Professor Guthmann's clinic at Frankfurt.

It was not, however, till three years later that the author had opportunity of studying more fully the methods and technique of ultra-short-wave therapy at the great Frauenklinik at Erlangen. This happened after the first International Congress on ultra-short waves held in January, 1937, where Professor Wintz, head of the Erlangen Clinic contributed a paper of outstanding interest on their methods and results. This interested the author so greatly that a visit to the clinic was arranged.

The work at the Frauenklinik affords convincing evidence of the great importance and value of ultra-short-wave therapy in gynæcology. A large number of cases was seen, suffering from some form or other of pelvic inflammatory disease, many with the usual complications of parametritis, pelvic peritonitis, etc. In all these cases a deep thermal effect is the most important factor. Previous methods for producing homogeneous heating in the pelvis, including diathermy, were all found inadequate whether given internally by vaginal or rectal electrodes or by anterior and posterior electrodes. The fact is that in diathermy, thermal effect is superficial, the current circulating only in the skin and subcutaneous tissues and never reaching the pelvic organs.

Very impressive were the results achieved in acute pyosalpinx of gonococcal origin. At Erlangen cases with high temperatures and much constitutional disturbance were treated by small daily doses of ultra-short-wave therapy and the results were excellent. Pain was relieved at once, while temperatures even of 103° and 104° F. fell to normal after three or four treatments, and all subjective symptoms cleared up rapidly with the absorption of inflammatory exudate.

In several of the less acute cases operation had appeared to be inevitable and ultra-short-wave therapy was merely ordered as a

preliminary method, but it was frequently found that after six to seven treatments the inflammation had subsided so completely that operation could be dispensed with. In other cases short-wave therapy definitely improved matters but the adnexal mass persisted on palpation. These were operated on successfully and convalescence was much more rapid than in those who had not been treated previously.

A large number of cases of adnexal disease in the sub-acute stage were having treatment. In most of these, cervical smears had given a definite positive reaction, in others pus cells were present. Some had sub-acute endocervicitis and cellulitis with considerable thickening of the tubes which were tender and painful. Most of these had a great deal of abdomino-pelvic pain with temperatures of  $90^{\circ}$  to  $100^{\circ}$  F. Amongst these were 5 cases of post-abortal sepsis with large tubal-ovarian masses. Three of these were due to initial adnexal infection while two were cases of acute exacerbation of a chronic inflammation. All of these were treated by the usual abdomino-sacral technique.

### Technique

Technique is of great importance in pelvic work and is carried out at Erlangen with minute efficiency. The great research laboratory of the Siemens works is situated only a stone's throw from the Erlangen clinic so that Professor Wintz and his assistants are in constant consultation with the heads of the laboratory staff and with Professor Patzold, and many innovations and improvements in technique are the result.

### Machines

The accompanying diagram gives an idea of the Siemens' Ultratherm, a valve machine of fairly adequate output, over 300 watts, with one wavelength of 6 metres. With this machine,

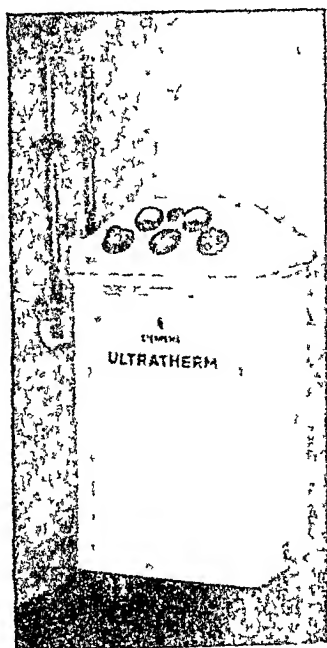


FIG. 70. Siemens' "Ultratherm."

very valuable results are obtained in acute and chronic adnexitis and other conditions.

When dealing with fibrous masses, hard nodules, tumours and dense adhesions better results are obtained by the use of Professor Wintz's favourite machine, the Ultra-Pandoros, with its output of over 650 watts and a larger choice of wavelength. The wavelength chiefly used at Erlangen for these cases is very short, approximately 3.70 metres. Professor Wintz considers that the shorter the wavelength the greater the penetration, provided the output is adequate.

Other important factors in technique are the position of the

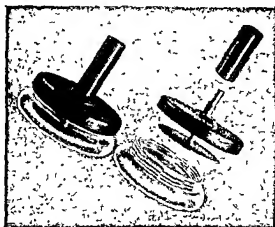


FIG 71. Schliephake's Glass shod Electrodes.

patient, the concentration of the current throughout the part treated; the electrodes, their nature, size and position. For pelvic work Schliephake's glass shod metal electrodes should be used exclusively as rubber and felt absorb too much energy. The air spacing must be wide to get the true depth effect. In placing electrodes it is important to get all the organs of the true pelvis, bladder, uterus, adnexa, and parametric tissues, into the condenser field. The best method is to use two large dorso-ventral electrodes of about 18 cm. diameter, the ventral electrode completely covering the pelvis, the dorsal electrode protruding below the coccyx. A common fault is to place the latter too high up in the lumbar region so that the electrical field only traverses the upper part of the organs. Three conditions are necessary for depth effect :

both electrodes should be placed at equal distances from the body; both should be of equal size; and concentration of the current on any prominent part must be avoided.

### Position of Patient

The patient either lies on a couch on the sound side, the side to be treated being uppermost in order to avoid concentration on the posterior electrode, or else she is placed in the supine position on the Erlangen Couch, an admirably constructed couch of latticed wood, with one electrode behind the sacrum, the other

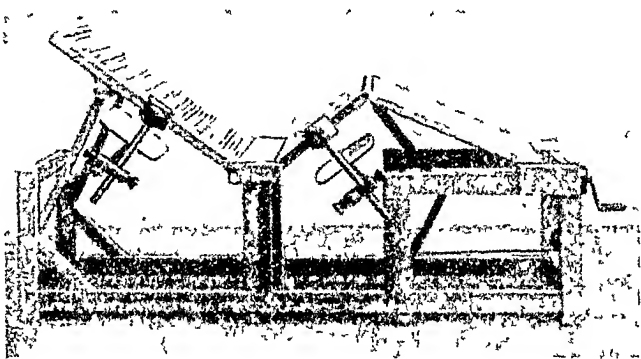


FIG. 72. The Erlangen Couch.

behind the flexed thighs. Failing this, which is an expensive affair, a canvas deck chair is suitable.

### Dosage

A practical, simple and exact dose meter is used at Erlangen. It is being investigated in England, but in many hospitals as yet dosage is roughly worked out on time and skin-electrode distance. Over-dosage must be avoided in acute cases where it is well to begin with short treatments of five minutes with distances of 10 to 15 mm. Strong treatments at this stage inevitably produce pain. Energy output must be kept low and only the very mildest degree of warmth, or athermic treatment, should be experienced. Daily treatments with occasional rest are given to acute cases and the time is increased cautiously up to fifteen minutes. After ten days, treatment is given thrice weekly.

In chronic cases dosage is much higher, for these cases need heat, and begin, with ten minutes' treatment given every other

day and prolonged to thirty minutes. The energy output is much higher because it is sometimes necessary to give slight temporary stimulation to a chronic condition.

In chronic cases dosage is much more difficult and athermic treatment practically useless. Professor Wintz is emphatic in stating that only specialised medical judgment and experience can solve the problem of giving enough heat to stimulate the healing process without overdoing it and breaking down nature's own defence mechanism.

Prognosis in these cases depends on whether the condition is mainly the result of inflammation or due to the presence of hyperplastic cicatricial tissue and chronic induration associated with adhesions which deform the tubes and cause much pain. In the latter cases short-wave therapy alone cannot effect a cure.

It is sometimes impossible at a first examination to decide which of these elements is the predominating factor. If in doubt it is the rule at Erlangen to give a preparatory course of six to eight short-wave treatments. These may not replace ultimate operation but never do any harm and always result in a clearer picture being formed of the true pelvic condition. Many inflammatory pelvic adhesions are removed by this, also swelling and chronic stasis, and then it is easy to recognise the hard exudate and adherent masses in the region of the broad ligament as well as larger cyst-like accumulations of fluid that only operation can remove.

Where the inflammatory picture is predominant the results of short-wave therapy in these cases are most satisfactory, a course of twelve to eighteen treatments often resulting in complete disappearance of any trace of a tubo-ovarian mass.

### Temperature

Temperature measurement in the pelvis during treatment by short-wave therapy has been the subject of much discussion. With the pelvis in the condenser field a rise of only 0.5° to 0.9° F. can be measured by a special thermometer of quartz and benzol, for mercury cannot be used here. As it has been found that various strains of gonococci survive a temperature of 106.7° F. it would seem that nothing short of the drastic methods used by certain American writers would suffice to eradicate them from the infected area. These writers combine general fever therapy with a rise of general temperature to 105° F. with a local diathermy treatment heating the vagina up to 109° or 110° F. Professor

Wintz doubts the advisability of applying such heat, either general or local. In his opinion a moderate local rise of temperature in the infected area is the important factor, and he considers that the actual damage done to the invading organism counts for less than the biological reaction of the patient and the renewed cellular activity caused by hyperæmia. In his opinion there is more in short-wave therapy than mere heat production, and, that though "specific effect" is not a very happily chosen term and has been a stone of offence to many, we cannot refuse to recognise other effects that exceed those of heat alone.

Much work and research is still necessary on the technical side in gynæcological work. War conditions are at present very unfavourable to this, but we should aim at the production of apparatus of greater power which may at least give the objective proof of "specific" effects. Above all the difficulty of exact dosage must be overcome.

In the Physiotherapeutic Department of St. Mary's Hospital a great deal of gynæcological work is done and the Erlangen technique is followed with very satisfactory results. Four Siemens machines are at work in wards and Out-Patients' Department all day long. One or two cases treated there during recent years may be of interest.

One of these was that of a young woman of thirty who had been delivered of a healthy child ten days before she was seen. She had a temperature of  $103.4^{\circ}$ . The general condition was bad, pulse feeble and rapid. There was severe pelvic pain and during the last twenty-four hours she had had several attacks of nausea and vomiting. The diagnosis was adnexitis, with parametritis on both sides, and pelvic peritonitis. There was tenderness all over the lower abdomen and in the region of both tubes. On examination a large inflammatory mass was found on the right side, on the left a tumour the size of a duck's egg. It was resistant and very tender to pressure. The sedimentation rate was high. A short-wave apparatus, the "Radiotherm," 350 watts, was installed and a short three-minute treatment given to each side with skin-distance of 10 cm. The result of that short treatment was that pain was relieved and the local inflammation began to abate. On the third day the temperature was normal. Sixteen treatments in all were given, gradually increasing the time up to twenty minutes on each side. At the end of a week there was neither pain nor temperature. In another week the patient was able to get up and go about, although there was some exudate



and local thickening. A fortnight later the ovaries were no longer adherent and the tubes not sensitive to pressure. Since then the patient has remained quite well.

Another case of chronic pelvic inflammation following abortion is instructive. The patient was a young woman of twenty-eight, and the case one of pelvic inflammation following abortion while travelling in the East three months previously. The patient complained of constant pain in the back and of pelvic pain, increased by standing, talking or any exertion. The whole lower abdomen was tender, especially on the right side, where a tubo-ovarian inflammatory mass was left, fixing the uterus to the pelvic wall. Any attempt to move this caused pain. A smaller tender mass was present on the left side. The patient looked very ill and distressed. She was treated in the usual way with short treatments of five to ten, later to twenty, minutes each side. Treatments were given in a deck chair with the "Ultra Pandoros" as rather dense adhesions were present. Treatment could only be given thrice weekly as the patient lived at some distance, so the pain, though lessened, persisted rather longer than in the case where daily treatment is given. It still came on after any undue exercise or fatigue, and there were occasional exacerbations. Menstruation always produced a good deal of pain, but progress was steadily maintained, and at the end of twenty treatments pain had disappeared. Her health had improved considerably and there was no trace of inflammatory swelling in the pelvis. This was confirmed by a gynæcologist who gave the patient a guarded prognosis regarding the possibility of another pregnancy within the next six months or more as the tubes were unlikely to be patent. Pregnancy did, however, occur within the next few weeks, which was a joyful surprise for all concerned, and in due time a healthy baby was born.

Another case was one of chronic pelvic inflammation following appendicitis. A young woman, married two years, complained of very severe dysmenorrhœa, especially marked on the first, third and fourth days of the periods which were irregular, now early now late, and much too profuse. There was no vaginal discharge and micturition was normal. She was very anxious to have a child. Her history was of an acute appendix two years previously, followed by drainage for three weeks. On examination a left tubo-ovarian mass the size of a large orange was felt. It was very tender. The uterus was retroverted and fixed, with many adhesions to the left and posterior to the uterus. There was some swelling of

the right fornix. Ultra-short-wave treatment was given. After ten treatments the tenderness had disappeared and the left mass was much reduced but still palpable, and the patient had had one menstrual period with very severe pain. Eight more short-wave treatments were given. The next two periods were painless, and very soon after, a six-weeks' pregnancy was diagnosed. The uterus was still retroverted and fixed. Six weeks later a twelve-weeks' pregnancy was found and the uterus was in its natural position. The points in this case were the following : (i) The initial severe pelvic inflammation, so severe that nothing short of laparotomy could have been considered if short-wave treatment had failed. (ii) The severe menstrual pain after treatment began. This is a very common occurrence and patients should be warned about it. (iii) The great relief of pain during subsequent periods. (iv) The fact that further improvement occurred in the pelvis for at least two months after short-wave treatment had stopped.

### Endocrine Disorders

These offer a promising field of work for short-wave therapy, and the deep hyperæmia in the pelvis appears to stimulate the secretory glands to higher function.

In ovarian hypoplasia, with scanty and irregular periods, and in amenorrhœa, especially where the uterus is small and immature, the writer has found direct treatment of the pelvis by this method satisfactory. The important thing is that there is no risk of possible damage to the follicle during its stages of evolution to the mature corpus luteum. This cannot be said of X-ray treatment for this condition.

Realising the direct control of the ovary by the anterior pituitary, and after reading Raab's excellent paper read at the Vienna Congress on this subject, the writer has successfully treated three cases of hypoplasia by treating the pituitary only with ultra-short-wave. The results were as good as those achieved by direct treatment of uterus and ovary. Raab also recommends the same treatment for dysmenorrhœa.

In a condition of such varied etiology as dysmenorrhœa it is difficult to assess the value of short-wave therapy. In general, it may be said that in dysmenorrhœa without gross pelvic lesions especially when spasm of the uterine walls is responsible for pain, and whether or not the condition is due to endocrine dysfunction, short-wave therapy has extremely good results. In these cases

the writer finds the abdomino-sacral method more successful than treating the pituitary only.

### THE GALVANIC CURRENT IN GYNÆCOLOGY

Leucorrhœa, due to cervical infection, is successfully treated by cervical diathermy by the Cumberbatch method. This, in the writer's opinion, is the one gynæcological condition where diathermy is superior to short-wave treatment, whether the infection be gonorrhœal or due to puerperal or other infection. Here and there one comes across a case that does not clear up on diathermy alone; such need the stimulating tonic effect of zinc or copper ionisation of the cervical canal completely to remove erosions and discharge.

Zinc and copper ions are also of use in some obstinate cases of vulval pruritus of menopausal origin. These are often so obstinate that every other treatment fails, even X-rays and ultra-violet light. Ionisation is of little or no value in anal pruritus; here, when such factors as hæmorrhoids, *B. Coli* or other bowel infection, have been excluded, strong doses of ultra-violet light by compression treatment with the Kromayer lamp show good results. In both these conditions the writer has had the best and most permanent results by combining physiotherapy with follicular hormones in high dosage. By this method several severe cases of menopausal pruritus have been cured in a comparatively short time.

Conditions of space forbid more than the mention of the great value of massage and exercises as an adjuvant to short-wave therapy and light treatment in gynæcological and obstetrical cases.

### ACTINOTHERAPY IN GYNÆCOLOGY

The writer is convinced of the great value of general irradiation by ultra-violet, visible and infra-red light in gynæcological cases.

The menstrual cycle and pregnancy represent biological processes that cause far-reaching changes in the endocrine glands; greater still are these changes in gynæcological disease of any kind.

These endocrine changes, again, influence the sympathetic nervous system and with it the three systems so closely related to it, viz., skin, connective tissues and musculature. Any endocrine disturbance soon manifests itself in the appearance of

sufferers from chronic pelvic disease. Their skins are harsh and dry, their faces sallow, their muscles poorly developed.

Conservative therapy must take all this into account; it is not enough to promote hyperæmia and cell regeneration in the pelvic organs; that great organ, the skin, must also be flushed with blood and its stores of hæmoglobin and minerals enriched. By means of general light baths, radiant energy is stored in the blood and carried to the tissues with renewed phagocytic and immunising power.

The regenerative process thus set up speedily manifests itself by improvement in skin, hair and general muscle tone, by increased appetite and gain in weight. General radiation is a wonderful aid to the removal of toxins—under its influence neurasthenic symptoms, the inevitable accompaniment of chronic pelvic disease, clear up rapidly, and fatigue, irritability and depression vanish.

There are many gynæcological conditions where ultra-violet light increases the effect of short-wave therapy. Ovarian hypoplasia is an important one, for it is one of the causes of sterility, and we can greatly aid both substitution therapy and short-wave therapy by general light baths. This treatment is also of use in dysmenorrhœa when hypoplasia is the cause.

### Actinotherapy in Pregnancy

A great adjuvant to short-wave therapy in gynæcology, actinotherapy becomes a vital necessity in the treatment of the expectant mother whose mineral stores are depleted by the inroads made on her own calcium and potassium. This is very noticeable during the eighth and ninth months when bone formation in the foetus is at its height and the mother's skin loses its elasticity: it is then that the tendency to œdema becomes marked.

Guthmann and Schol have shown that calcium is stored in the blood by ultra-violet light and that ten to twelve general light baths given to the mother at this period will restore her calcium balance and also increase the production of vitamin D for the benefit of her offspring.

Light treatment need not be expensive or difficult in gynæcological work. In former years great use was made abroad, and by the writer, of Landeker's carbon arc lamp which combined internal radiation of the whole abdomen with visible and infra-red light. It was, however, expensive and complicated, and short-

wave therapy has greatly simplified physiotherapeutic treatment of gynaecological cases.

The simplest and most inexpensive light equipment for a gynaecological department is a mercury vapour Hanovia lamp with a Sollux which has a spectrum rich in visible and infra-red rays.

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